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TO THE
LOCAL GOVERNMENT BOARD
ON
PUBLIC HEALTH AND MEDICAL SUBJECTS.

(NEW SERIES No. 43.)

Dr. J. C. G. Ledingham's Report to the Local Government Board on the Enteric Fever "Carrier"; being a review of current knowledge on this subject.

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Arthur Newsholme,
Medical Officer,
5th October, 1910.

PREFACE.

Although the discovery of the "carrier"* as an agency in the transmission of enteric fever is a comparatively recent event, the literature of this subject has already attained large dimensions. This result is due to more than the interest created by the detection of a previously unrecognised channel of transference of the disease; it is, in great part, owing to the belief that the carrier is more than a mere transmitter of infection.

In the earlier days of bacteriology, with increasing bacteriological knowledge had come increasing difficulty in understanding how and where the infective organism of enteric fever maintained its vitality between the recognised occurrences of the disease, whether in the form of epidemic outbreaks or in that of endemic prevalence, to which it gave rise. Some degree of explanation, no doubt, was to be found in the probable existence of unrecognised cases of the fever, which might serve to secure the life-chain of the organism, but this hypothesis was not regarded as sufficient in itself. It came, accordingly, to be considered probable that the organism led a saprophytic existence outside the human body, and was capable of living and multiplying in such inanimate media as water and soil. This hypothesis at first received considerable support from bacteriologists, but as the result of further investigations fell largely into discredit. Following on this, came the discovery of the carrier, and with it the view that the

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* A "carrier" of enteric fever is a person who, although he may be in good health, carries the infectious material of the fever in his body, from which it may be given off in the stools or in the urine.

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carrier of enteric fever is not, like inanimate agencies, a merely passive transmitter of infection, but is a breeding ground and storehouse of the specific organism of the fever. These organisms live and flourish in his body, from which they may, whether continuously or from time to time, be excreted and give rise to the disease in others.

It appears, therefore, that not only persons sick with the fever, but also healthy persons who are carriers may infect others. It is contended that, by these two cycles of infection, the continued existence and infectivity of the enteric fever organism can be largely, if not wholly, explained without need for assumption of long viability of the organism outside the human body.

A hypothesis of this importance naturally attracted much attention and led to many investigations of the question. The results of these investigations are to be found in numerous publications by the observers who, in different countries, have been working in this field. But to obtain access to these widely scattered publications is a matter of no small difficulty, and accordingly Dr. Ledingham, who, along with myself, is engaged, on behalf of the Board, in an inquiry into protracted and recurrent infection in enteric fever, considered that there would be advantage in preparing for publication a summary of at least the more important investigations that have hitherto been made in connection with this subject.

In the accompanying report by Dr. Ledingham a summary of the sort is given. A considerable part of the report is devoted to the literature of the question of principal importance, that, namely, of the infectivity of carriers. Dr. Ledingham gives the history of a large number of occurrences of enteric fever in domestic life, in institutions, and in military populations, in which the source of infection has been traced, more or less convincingly, to a carrier. In many of the examples that he quotes, the evidence incriminating the carrier is conclusive. The infection was conveyed from the carrier to his victim, in many instances, by food or milk, while, in not a few others, the personal relationship between the carrier and the person attacked was sufficiently close to suggest direct personal infection. What share of enteric fever is directly due to the carrier is a problem which has been investigated by several observers, and the results of their investigations vary markedly. The proportions recorded by different inquirers range between 2·3 per cent. and 32 per cent. of the total amount of the fever. Some of those who have obtained the higher figures maintain that their results were due to more careful and sustained investigation and are the more accurate.

In view of the potential danger of the carrier to the community in which he lives, it is of interest to know what proportion of these persons exists. In this connection, Dr. Ledingham sets out the results of investigations undertaken with a view to ascertaining the degree of frequency with which carriers, whether those in whom the condition lasts but a short time (transitory carriers), or those in whom it is more permanent (chronic carriers), have been found in certain groups of persons. These investigations were made in relation with persons who had recently had enteric fever, with persons known to have been in contact with cases of the fever, and with an ordinary population. The results show considerable variations, perhaps partly dependent upon the differing degree of frequency with which bacteriological examinations were made and on the varying degree of efficiency of the methods employed. Moreover, it cannot be said that investigation of this kind has yet been made on such a scale, or with such allowance for the varying circumstances of different populations, as to justify definite conclusion. Such as they are, the results go to show that the proportion of carriers in an ordinary population is about 3 or 4 per 1,000 ; but, for the reasons given, these figures cannot properly be regarded as affording a trustworthy indication of the true proportion of carriers in communities generally.

Dr. Ledingham also discusses the nature of the carrier state and refers to interesting observations that have been made in this connection. He cites statistics which show that, so far as present data go, the chronic carrier condition appears to be much more frequent in adult life than in youth and in the female sex than in the male sex. In the latter connection he considers the association that has been observed between the carrier state and gallstone disease, and the apparently greater liability of women to both these conditions.

A question of practical importance, which Dr. Ledingham treats with considerable detail, is that of the possibility of effecting a cure of the carrier condition. He gives an account of many instances in which curative treatment of the carrier, whether by drugs, vaccines, surgical operation, or in other ways, has been attempted. It has to be confessed that, so far, the results of such treatment have not been encouraging. There would seem to be somewhat more hope of effecting a cure of the urinary carrier than of the intestinal carrier ; as regards the latter, the prospect of success, in Dr. Ledingham's view, is, save perhaps in the early stage of the condition, extremely remote.

The measures that have actually been taken, or that have been suggested as suitable for adoption, with a view to lessening the danger of dissemination of enteric fever by carriers, form the subject of the last chapter of Dr. Ledingham's report. They consist, in the first place, of taking such action as is likely to lead to the detection of carriers in the community, and, in the second place, of endeavouring to secure, on the part of the carrier, the observance of such precautions as are calculated to minimise the risk of his infecting other persons. Foremost among these stands the necessity of the strictest personal cleanliness, especially as regards the hands. Safe disposal of the infectious excreta is also a matter of much importance. There is no legal provision enabling the carrier to be debarred from undertaking what occupation he pleases, notwithstanding the fact that a carrier who is engaged in the milk trade or in the preparation or handling of food may be a public danger. In the absence of power to exclude the carrier from such occupations, endeavour should be made to attain this end by persuasion, and, in the event of failure to persuade, to secure the strict and continued observance of every possible precaution on his part.

THEODORE THOMSON.

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CHAPTER I.

INTRODUCTORY.

In the campaign against infectious diseases, no knowledge can be of greater importance to the epidemiologist than that which springs from a correct understanding and appreciation of the natural history of the infective agents, whether bacterial or protozoal. It is only within the last decade that the active co-operation of the epidemiologist with the bacteriologist and parasitologist, has led to a much clearer insight into those factors which influence the rise and spread of epidemic diseases. As evidence of such fruitful co-operation, one has only to cite the progress which has been made in our knowledge of the spread of malaria, sleeping sickness and Malta fever. When we come to those bacillary infections associated with disturbances of the intestinal tract (typhoid fever, paratyphoid fever, dysentery, cholera, &c.), we find that up to quite a recent period, most attention was directed, and rightly so, towards rendering innocuous what were recognised to be at least temporary harbourers, if not permanent hosts, of the bacilli. These hosts were almost invariably of inanimate nature (water, soil, air, food, &c.), but much of the evidence on which was based the belief that such hosts constituted permanent seats of vegetation of the infective agents, has now been proved to be erroneous or of an unconvincing character. It is becoming more and more evident in the case of the diseases referred to, that the main habitat of the infecting agent is to be found in the animal organism itself, where it has found a temporary or prolonged lodgment.

In this memoir I shall be concerned solely with the typhoid bacillus and its recently recognised property of leading a saprophytic existence in an organism which may or may not react to its presence in any obvious fashion.

To Robert Koch (1902) must certainly be given the credit of pointing out clearly the necessity of rendering the typhoid patient innocuous to those in contact with him, by efficient disinfection of the excreta, both during the disease and in convalescence, by careful enquiry into, and supervision of the ambulant and abortive cases, and especially of those anomalous types met with so frequently in children.

At Koch's recommendation bacteriological stations were instituted in the typhoid-ridden districts, notably in south-west Germany, for the purpose of testing in actual practice the validity of his dictum that the chief source of typhoid infection is to be found in man himself. These institutes have proved fruitful not only in helping to check the further spread of epidemics already arisen, but also in explaining the causation of many epidemics the source of which could not be traced to contact with the typhoid patient, or to other commonly recognised agencies of infection. In fact, the discovery of the typhoid-carrier was a natural sequence of the systematic bacteriological examination of the typhoid convalescent. That persons apparently quite healthy could harbour typhoid bacilli after an attack of the fever, emit them continuously or periodically in the excreta and thus act as potential sources of infection, was a new fact in the etiology of enteric fever. It had certainly been demonstrated several years previously that the typhoid bacillus might remain for long periods in the gall-bladder, bone-abscesses and other situations, but the exact significance of such finds from the epidemiological point of view had not been thoroughly realised. Such findings, so far as they concern us here, will be referred to in their proper place (*vide* Chap. VII). The true typhoid-carrier, by which is understood a person who excretes the typhoid bacillus continuously or intermittently in the fæces or urine, will demand the greater part of our attention in this monograph.

As much of our knowledge of the typhoid-carrier subject has emanated and still continues to emanate from the bacteriological stations in south-west Germany it may be well here to refer briefly to their constitution and scope of work.

In thus giving prominence to the efforts of the hygienists and bacteriologists in the south-west Germany campaign, I do not wish it to be implied that the discovery of the carrier-condition was entirely a German product or even that the epidemiological importance of the carrier was first grasped by the Koch school. The intestinal carrier—the most important because the most frequent type—undoubtedly came to light as the result of the German campaign-work; but the chronic urinary carrier—the much rarer, though probably more dangerous type—was known (*vide* Chapter X.) at least two years before Koch's famous address in November, 1902, and in this country Horton-Smith (1900) had already called attention to the etiological importance of the latter in his Goulstonian lectures in 1900. There can be no question however, that it is to the concentrated efforts of the German typhoid-campaigners that we owe the larger part of our material for this new chapter in the etiology of typhoid fever.

In the flat south-western portion of Germany, typhoid fever had become so prevalent, particularly in the Regierungsbezirk Trier, the Bavarian Pfalz, and in Alsace-Lorraine, that a general spread of the disease by the floating industrial population of this district to all parts of Germany began to be dreaded. On Koch's recommendation an experimental typhoid station was planted at Trier in 1903, under the directorship of Frosch. Such excellent service was rendered by this station in elucidating the spread of enteric fever, that it was determined to increase largely the number of such institutes where co-operative epidemiological and bacteriological work could be carried out. Full information with regard to the site, organisation and scope of work of these stations is to be found in a Preface to Volume XXIV. of the Arbeiten aus dem Kaiserlichen Gesundheitsamte, and more shortly in the Festschrift presented by the Imperial Board of Health to the Berlin Hygiene Congress of 1907. Further notes will be found in the individual reports of the stations and in the general statistical reports of Frosch (1907-*b*), Schneider (1907), Kirchner (1907), and Klinger

(1909), which will be further referred to.* According to the latter there were in existence and in full swing in the year 1907, eleven such stations with a staff of 35 bacteriologists attached to them.

The institutes were situated at the following places :—

Trier	Prussian stations in the district of Trier.
Saarbrücken	
Saarlouis	
Neunkirchen	
Kaiserslautern	Bavarian stations in the Pfalz district.
Landau	
Idar	...In the Fürstentum of Birkenfeld.
Strassburg	In Lower Alsace,
Hagenau	
Metz	In Lorraine.
Diedenhofen	

The population of this district was about 3,186,000, distributed in 3,240 Gemeinden (communities). The following facts with regard to the constitution of the stations have been extracted practically verbatim from the official Congress Festschrift above referred to (pp. 114, 115, 116).

The typhoid stations are provincial establishments. To ensure uniformity of action and co-operation among them, an "Imperial Commissioner for the typhoid campaign in the south-western portion of the Empire" was appointed in November, 1904, with his headquarters at Saarbrücken. For Bavaria a District Commissioner was entrusted with this duty. In the execution of his office this official would have the assistance of the respective municipal authorities. He has to supervise the general hygienic conditions of his district so far as they may have concern with the spread of enteric (*e.g.*, drinking water, sewage disposal, housing, &c.) and point out deficiencies therein.

For this purpose a medical advisory officer is accredited to his staff.

With regard to the stations, by a special arrangement with the Imperial Administration and that of the confederated States, a definite line of action or "reference" (Dienstanweisung) has been drawn up in which it is expressly stated that their chief task is the bacteriological examination of suspected material from patients with a view to accurate diagnosis. The medical men at these stations are empowered to prosecute their enquiries on the spot in conjunction with the official authorities. In searching out concealed cases, they will have at their disposal the police notifications of strangers in the district, the school absentee lists, dispensary lists, the official death notifications, the lists of employees in manufactories, &c. Further they may derive information from the clergy, the school teachers, and the midwives.

The aim of these enquiries is to search out as early as possible all typhoid cases and carriers, to explain the source of infection in each case, to take active measures against the existing focus of infection, and to prevent the further spread of the disease.

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* The organisation of the campaign and the results achieved have been dealt with recently by Lentz in a paper read before the Section of Bacteriology, Brit. Med. Assoc., London, 27th July, 1910.

The directors of the stations have to co-operate with the official health officers, practising physicians and police and parish officials and to accommodate themselves to the directions of the local authorities. They must keep themselves continually informed as to the hygienic conditions of the district and other conditions relative to the occurrence and spread of enteric fever.

Every three months the Institutes make a report to the District Chairman and to the Imperial Commissioner, who presents a return to the Imperial Board of Health.

Special instructions are also given with regard to notification, diagnosis and prevention of the spread of enteric fever. From these I make the following extracts :—

1. Notification must be made not only of undoubted cases of typhoid fever but also of cases suspected to be typhoid fever.

2. In the diagnosis of the disease, the assistance of the director of the bacteriological station as well as of the official health officers should be requisitioned. These should have access to the sick-bed so far as the medical attendant considers advisable in the interests of his patient.

3. Among the measures to prevent the spread of the disease, the removal of the sick and of suspected cases is provided for. Persons excreting typhoid bacilli, but who present no symptoms or only slight symptoms of typhoid fever (so called Typhus-bazillenträger), and convalescents who are still discharging the specific bacilli, should as far as possible be dealt with as sick persons.

Where no legal right exists for this purpose, or where for other reasons (interference with occupation, &c.) such a measure is impracticable, one should by oral and written instructions urge upon these carriers the necessity of disinfecting their excreta and their washing, and convince them that by neglect of these precautions they run the risk, not only of re-infecting themselves, but also of continuously giving rise to fresh cases in their vicinity.

Typhoid patients should be taken to hospital and should be isolated there until two examinations at weekly intervals demonstrate the absence of typhoid bacilli from their excreta.

Where possible, isolation should continue until a third examination, made after another week, has proved negative. Suspected contacts should be kept under observation for three weeks, and, when circumstances demand it, also examined bacteriologically.

In the following chapter I shall deal with the general data regarding carriers, collected from the reports of individual institutes and official campaign statistics in Germany and other countries.

CHAPTER II.

GENERAL FACTS REGARDING CARRIERS.—AGE, SEX, FREQUENCY, &c.

The earlier efforts of the typhoid institutes in south-west Germany contributed an enormous amount of information on the part played in the spread of typhoid fever by contact of the affected person with the healthy, and abundantly confirmed the views promulgated by Koch. An excellent account of the investigations at Trier during the earlier months of the campaign is given by Frosch (1903) and at Saarbrücken by Drigalski (1904). These investigations, together with those of Dönitz (1903) in Berlin, served to illustrate the significance of atypical enteric fever in children, and of the ambulant, abortive, or completely unrecognised types of the disease. Although, however, contact infection from the sick to the healthy was a powerful, if not the most powerful factor in the spread of enteric fever, they found that there was a fairly large quota of recurrent outbreaks of typhoid fever, mostly confined to isolated houses or groups of houses in country districts or streets, where no such contact with an obviously sick person could be traced. This circumstance, together with the knowledge acquired many years before, that the typhoid bacillus might in certain cases remain for long periods in the body in association with bone abscesses, cholelithiasis, &c., led Frosch to put forward the suggestion that possibly in the intestinal tract also the infective germs might lead a saprophytic existence, and by their intermittent discharge into the outer world lead to further infection. Frosch's suggestion was a happy one, and has been entirely confirmed not only by the subsequent investigations in south-west Germany but in all countries where the subject has received attention.

To Drigalski (1903 and 1904) belongs the merit of establishing on a bacteriological basis the hypothesis put forward by Frosch, then Director of the Typhoid Commission, that the B. typhosus might in certain cases lead a prolonged saprophytic existence in the human intestine. When he wrote the account of his experiences at Saarbrücken, this institute had been in existence only ten months. During that time he had been much impressed by the repeated occurrence of enteric fever in certain houses and in towns where the sanitary conditions appeared quite satisfactory. To explain this phenomenon he had to assume the possibility of a prolonged existence of the typhoid bacillus outside the body, but this view he very soon abandoned in consequence of the bacteriological results he obtained in a series of typhoid cases. The stools in 64 cases of typhoid fever were examined bacteriologically at different times during the disease and also during convalescence with the following results :—

Time.	Typhoid bacilli present.	Percentage.
1st.—5th day of the disease...	10 cases. ...	15·6
6th.—10th „ „ ...	15 „ ...	23·4
11th.—20th „ „ ...	21 „ ...	33·0
21st.—27th „ „ ...	8 „ ...	11·5
After 8-10 weeks	7 „ ...	11·0
After 3 months and later ...	3 „ ...	4·7

The longest time during which the B. typhosus was demonstrable in the stools was 14 weeks, and in a footnote, referring to a later date, he observes that in this particular case the bacilli were still present at the end of nine months when they formed 50–60 per cent. of the total flora. This case would, therefore, constitute the first recorded chronic carrier traced from convalescence onwards. He was also further successful in discovering a chronic carrier in the person of a Hausfrau who apparently had never suffered from typhoid fever.

Some of these facts which had been detailed a few months previously by Drigalski at a scientific meeting, together with certain parallel observations on convalescent urinary carriers made by Dönitz (1903) in Berlin, had afforded a reasonably strong foundation for the hypothesis formulated shortly afterwards by Frosch.

Before proceeding to detail the systematic bacteriological investigations which have enriched our knowledge of the carrier question, it may be well to refer briefly to the facts which have accumulated regarding the excretion of typhoid bacilli by the typhoid patient during the course of the disease.

In the first place with regard to the faeces, it would now appear that the proportion of instances in which the typhoid bacillus may be detected in the faeces at one or another stage of the disease depends almost entirely on the degree of efficiency of the bacteriological methods in current use. I have already referred to the earlier data of Conradi whose highest percentage (viz., 33 per cent. in a series of 64 cases) was obtained during the third week of the disease, whereas in the first five days only 15·6 per cent. were positive. Much higher values than these have been recorded of late.

Brion and Kayser (1906) examined a series of 144 cases during the febrile period with the following results :—

1st week.	Cases examined	22.	Positive	7	=	32 per cent.
2nd „	„ „	51.	„	18	=	35 „
3rd „	„ „	71.	„	31	=	45 „

Bohne (1908) examined 27 cases, and obtained the highest percentage during the fourth week, but his series is too small for statistical purposes.

1st week.	Cases examined	2.	Positive	0	=	0 per cent.
2nd „	„ „	13.	„	3	=	23 „
3rd „	„ „	7.	„	3	=	43 „
4th „	„ „	4.	„	4	=	100 „
5th „	„ „	1.	„	1		

By the aid of the more recently introduced media (see Chapter XI.), Gaehtgens and Brückner (1910) have obtained, in a series of 72 cases, the following results which may be considered the best attainable at the present time:—

1st week.	Cases examined	21.	Positive 12	= 57 per cent.
2nd ,,	,, ,,	32.	,, 17	= 53 ,,
3rd ,,	,, ,,	13.	,, 10	= 77 ,,
4th ,,	,, ,,	4.	,, 2	= 50 ,,
5th ,,	,, ,,	2.	,, 2	

To summarize, in about 75 to 80 per cent. of typhoid cases examined during the third week, typhoid bacilli are demonstrable in the faeces, and it is not unlikely that with further improvements in technique a still higher percentage will be obtained. I have not alluded to the demonstration of typhoid bacilli in the faeces during the incubation stage, but it is important to remember that in not a few instances (Mayer, G. (1903), Conradi (1907), Prigge (1909), &c.), the discharge of the specific micro-organisms at this early period has been proved beyond all doubt.

With regard to the urine, the isolation of typhoid bacilli, if present in this fluid, is, as a rule, a simple matter. Most observers are agreed that in about 25 per cent. of all cases of typhoid fever it is possible to demonstrate the bacilli in the urine. They appear generally in the later stages of the disease, after defervescence (Herbert (1904)), or in late convalescence, but they have also been found frequently at the period of eruption of the rose spots. Further data on this subject will be found in the Chapter on Urinary Carriers.

I now pass to the consideration of Lentz' (1905) results obtained in the course of his examination of typhoid convalescents, at his institute in Idar. Out of 400 convalescents Lentz reported that six continued to excrete the bacillus for a longer period than 10 weeks, dating from the beginning of the disease or from the beginning of a relapse. None of these six cases, however, continued to be infective for a longer period than 13 months, when repeated examination showed that the excreta were typhoid free. There was thus an apparent late cure in the bacteriological sense, but as we shall subsequently show, such "cures" must be regarded with great caution.

Though these six persons ultimately became typhoid free, 12 others did not rid themselves of the bacilli once they reached the chronic stage. The total percentage of carriers in Lentz' series was therefore 4·5 (1·5 per cent. temporary carriers and 3 per cent. chronic carriers).

The fact that these chronic carriers had been traced from the primary infection onwards, led Lentz to investigate all relatives and other persons who had been in association with typhoid patients as well as those persons who in previous years had suffered from typhoid fever. Twenty-two carriers were discovered by this method, 19 of whom were females and three males. The general health of the majority of these carriers was good, but three of the females developed gallstone disease, as was proved by the excretion of small stones in the faeces.

It is not possible to obtain accurate data regarding the previous history of every person who is discovered to be a carrier. As we shall see later, a large proportion of these carriers have not been found to present a history of known typhoid infection. Others again are able to supply data which at least suggest that they may have previously suffered from some form of ambulant or abortive typhoid fever, while others have been traced to the chronic stage right from the primary infection. Different terms have been employed by different authors, in the classification of carriers, but all, in the absence of further knowledge, must be considered somewhat artificial.

Conradi (1907) adopted the classification of Primary, Secondary, and Tertiary carriers. To the first group (Primary) belong those carriers in whom the infection has not led to the occurrence of symptoms of enteric fever. In this group Conradi includes those cases in which the excretion of typhoid bacilli has been found to take place during the incubation stage. The facts relating to this group will be fully discussed later.

To the second group (Secondary carriers) belong those who, having been attacked by enteric fever, continue to pass the bacilli for some time beyond a period of ten weeks from the commencement of the attack.

Out of 400 typhoid convalescents, Conradi got 22 secondary carriers (5·5 per cent. Compare Lentz' figure of 1·5 per cent).

To the third group (Tertiary) belong those who continuously pass the bacilli after the primary attack. Two tertiary carriers out of 400 convalescents were found by Conradi (equals 0·5 per cent. Compare Lentz' figure of 3 per cent.).

This classification of Conradi's is not to be recommended as the terms employed raise no clear idea in the mind as to the conditions they connote.

Sacquepée (1910) has recently suggested a more intelligible classification of carriers, thus :—

- Group I. *Porteurs précoces* (precocious carriers), *i.e.*, those who have taken the typhoid bacillus into the system but who as yet do not present any symptoms of infection. This group would consist only of carriers in the incubation stage.
- Group II. Persons who have recovered from typhoid or some typhoid-like infection, but who continue to excrete the bacillus whether for a short or for an indefinite period.
  - Sub-group A. *Porteurs convalescents*, in whom the excretion ceases before the end of the third month.
  - Sub-group B. *Porteurs chroniques*, in whom the excretion lasts for an indefinite period.
- Group III. *Porteurs sains* or *porteurs paradoxaux*, *i.e.*, those who have never had symptoms of typhoid fever, but who may excrete the bacillus over an indefinite period.

It will be seen that the primary carriers of Conradi include both the precocious and the paradoxical carriers of Sacquepée.

There is no doubt that this classification by Sacquepée is a fairly comprehensive one, but a sharp line of demarcation cannot always be drawn between Group I. and Group III. ; and probably many of the so-called paradoxical carriers would be found to fall into the category of the convalescent or chronic carriers if sufficient details as to their previous history were available.

For ordinary descriptive purposes we shall find that the terms "temporary" (or transitory) and "chronic" carriers are sufficiently explicit to denote the two great groups with which we have to deal. According to current German usage, convalescents who excrete the typhoid bacilli for not more than three months after the beginning of the disease are called *Bazillenträger* (or, shortly, transitory carriers), while those who excrete the bacilli for more than three months are called *Dauerträger* (or chronic carriers).

In the course of this survey we shall find that very important differences exist between these two great groups of convalescent carriers.

Having dealt with the figures of Lentz and Conradi, I now proceed to consider further data concerning the frequency of carriers.

Klinger (1906) of the Strassburg station instituted a bacteriological examination of healthy persons living in the neighbourhood of actual typhoid cases. 1,700 such persons were examined, with the result that 15 carriers were found during the period 1st July, 1903, to 31st March, 1905. These carriers were of all ages from 18 months to 60 years, and as to sex, seven were females and eight males. Of these 15 carriers, 11 had no clinical symptoms either before or after finding the bacilli. In nine of these 11 carriers the bacilli were found only on one occasion, but in the remaining two they were found three times in the course of a fortnight. All subsequent examinations were negative. Thus one might provisionally apply the term of "temporary," or as Klinger suggested, "acute," to these 11 cases (they were six males and five females). The other four carriers were of the chronic type (two males and two females). One had had enteric thirty years before, a second, 10 years before, while the remaining two were lunatics as regards whose previous illnesses no trustworthy information was available.

Klinger also gives a report of the examination of 482 cases of typhoid during convalescence (at the Strassburg station). Fifty-five or 11·4 per cent. of these excreted typhoid bacilli during convalescence, but not for a longer period than six weeks after defervescence, *i.e.*, temporary carriers. Eight, however, continued to excrete the bacillus beyond this period and thus fell to be reckoned as chronic carriers (= 1·7 per cent.).

In a later communication Klinger (1907) notes that of 604 convalescents examined, he had found 80 temporary carriers (70 or 11·6 per cent. intestinal and 10 or 1·7 per cent. urinary). Six cases only or 1 per cent. became chronic carriers. He states that the temporary urinary carriers were all cured by urotropin.

Another interesting series is reported by Kayser (1907), also of the Strassburg station. This author initiated a late control examination of the typhoid convalescents who had previously been discharged as typhoid-free during the period summer, 1903, to summer, 1905. This late control examination took place after the lapse of at least one year. The potential material for this test was 217 cases, but he was able to recover samples of stools and urine from 101 persons only (= about 46 per cent. of the survivors)

(33 men, 47 women, and 21 children). There had been 248 cases treated, but 29 of these had died. Of the remaining 219, one had died of another disease, and one had committed suicide. The result of this late examination was that three more carriers were discovered (two females and one male). In the previous year he had examined in conjunction with Brion (Brion and Kayser, 1906), the faeces of 200 convalescents and obtained a carrier percentage of 1·5. To show the importance of this late control test, the bacteriological findings in two of Kayser's cases may be quoted :—

Female (40 years)	July, 1904	Primary attack.
	Aug., 1904, 2 exams.	Negative.
	Oct. 4, 1905	Negative.
	Dec. 7, 1905	Positive.
	Jan. 18, Feb. 17, Mar. 9, 1906	Negative.
Female (26 years)	Aug., 1904	Primary attack.
	Sept. 23, 1904	Positive.
	Oct. 1, 1904	Negative.
	Dec. 7, 1905	Positive.
	Jan. 18, 1906	Positive.
	May 14, 1906	Negative.

In these two cases, therefore, the routine bacteriological tests made in early convalescence and before discharge, had proved inefficient owing to marked intermittency in excretion. This difficulty is a very serious one and militates greatly against any reasonably practicable system of bacteriological supervision before discharge. By this late control method, Kayser's percentage of convalescent carriers was raised from 1·5 per cent. to 3 per cent. or 5 per cent. I shall have occasion to refer again to the question of enormously prolonged intermittency in convalescent carriers.

A more recent report by Brückner (1910) on a similarly conducted investigation at the Strassburg Institute, shows clearly the necessity of the late control examination of typhoid convalescents. Kayser's material was derived from the town of Strassburg only, while Brückner also included four suburbs of Strassburg and eleven other townships belonging to his campaign district. The potential sources of material were 566 persons who had had enteric fever in previous years. Of these it was found that 45 (*i.e.*, 8 per cent.) had died and 170 (*i.e.*, 30 per cent.) had removed elsewhere or were not discoverable. There were thus left 351 persons, and only 35 of these (*i.e.*, 9·9 per cent.) declined to supply material for examination. This percentage would have been still lower had it not been for one small township in which 21 recovered typhoid cases resided, of whom 12 (*i.e.*, 57 per cent.) refused specimens. Brückner remarks that this low percentage of refusals is an index of the public appreciation of the efforts of the typhoid-stations. Among the 316 persons whose excreta were examined 12 carriers were found (= 3·8 per cent.), viz., nine typhoid carriers and three paratyphoid (B)-carriers. Of these 316 persons 104 were children (under 15 years) and 212 were adults (over 15 years). One carrier belonged to the former group and 11 carriers belonged to the latter group. The proportion of carriers among adults was therefore 5·2 per cent.

I append the following brief facts with regard to the individual typhoid carriers, as they show how important this question of intermittency has become :

1. Frau L. Had typhoid fever in summer, 1906. 19th June, faeces positive, urine negative. 27th July, faeces positive, urine positive. 1st August, faeces negative, urine positive. 13th August, faeces negative, urine positive. Further examinations on 17th, 21st, 27th August, and 17th October, 1906, were negative and Frau L. was registered as "bacteriologically cured." Now, in 1908, typhoid bacilli have been repeatedly found in her faeces, and once in her urine.

2. Herr L. Had typhoid fever in summer, 1906. During the period September, 1906, to April, 1907, he was regarded as a carrier, but as three negative examinations followed on 7th June, 23rd September and 27th October, 1907, he was struck off the list. Now on 11th December, 15th December, 1908, and 2nd January, 23rd January and 20th March, 1909, he is found to be discharging typhoid bacilli.

3. Male (58 years). Had typhoid fever in 1880 and was found to be a carrier in 1906. The discharge was found to be intermittent, but as the result of eight successive negative examinations, he was struck off the list in October, 1906. He is now actively discharging typhoid bacilli.

4. Female (32 years). Had typhoid fever in October, 1906. Discharged as "bacteriologically cured" after three negative examinations. Now her stools are positive (March, 1909).

5. Female (16 years). Had typhoid fever in 1906, and was discharged as typhoid-free. In February, 1909, her stools were found to contain typhoid bacilli. It was of interest that a sister of this case had also had typhoid fever about the same time in 1906, and had been a transitory carrier. The latter, however, is now (March, 1909) negative.

6 and 7. Two brothers (18 and 24 years) had typhoid fever in 1898. Now, in 1909, both are found to be carriers.

8. Frau R. (49 years). Had typhoid fever in 1899. Now found to be a carrier (March, 1909).

9. Male (31 years). Had typhoid fever in 1907 but was discharged as "bacteriologically cured." On 19th November, 1908, his stools contained typhoid bacilli.

In this list there are five males and four females—a relative proportion which is at variance with the usual experience. It has to be noted, however, that two of the males had already been known as carriers but had been struck off the list owing to repeated negative tests. Also in the two brothers (6 and 7) bacilli were found on one occasion only, while in No. 9 one examination only was possible. Further, in the male cases (with exception of 2 and 3), bacilli were as a rule very scarce, while in the female cases, they were being discharged in enormous numbers. Moreover, account has to be taken of the smallness of the series (viz., 9) at Brückner's disposal. Such small series are of little value for statistical purposes.

Perhaps the most thorough bacteriological investigation of typhoid convalescents hitherto reported has been carried out by the Central Research Institute at Kasauli in India, under the direction of Lieut.-Col. Semple and Captain Greig, with the assistance of Lieut.-Col. Thomson, Captains Harvey, White, Hodgson and Assist.-Surg. Paras Ram. (Semple and Greig 1908.)

This enquiry was set on foot in 1906 with the object of elucidating the incidence and spread of typhoid in the Indian cantonments, and one of the main problems attacked was the duration of the typhoid bacillus within the human host. Numerous observations were also made on the viability of the bacillus outside the human body, in urine, fæces, articles of clothing, &c., and the conclusion was arrived at that under natural Indian conditions its saprophytic existence outside the human host was a remarkably short one—a view which practically all modern work on this subject substantiates. In the case of convalescents the observers were not content with the prescribed German routine of two or three final examinations (at intervals of ten days after defervescence) of the excreta before discharge. All their convalescents were examined daily and many of the cases also, throughout the febrile period as well, until the excretion of the bacillus either ceased spontaneously or became chronic. In their report issued in 1908 they note that 86 convalescents had been examined at the Kasauli depôt, with the result that no fewer than ten persons were found to be excreting typhoid bacilli in the urine or fæces for periods longer than six weeks after defervescence. This gives the very high percentage of 11·6 of chronic carriers (taking the three-month limit and over as the test for the "Chronic" category). This is undoubtedly the highest percentage so far recorded and may probably be attributed in great measure to the elaborate routine by which it was scarcely possible to overlook an intermittent carrier. In civil conditions certainly, methods equally thorough would be impossible in practice.

Semple and Greig were working with a more or less homogeneous population, viz., adult males of a definite age-group. In order to determine whether this fact would in some measure account for the high percentage of carriers, I have taken the accumulated statistics of Klinger for the German campaign and determined whether in the age-group 23–45 it would be possible to obtain a percentage of 10 carriers in a small sample of 80 convalescents. The chances of this happening worked out at less than one in a billion, and one must, therefore, conclude that the high percentage they obtained was most probably due to the thorough routine they adopted.

At the close of Semple and Greig's report is a series of tables in which the results of the daily examinations of 18 convalescents are detailed. These tables are worthy of careful study, as they show how readily intermittent carriers may be overlooked by a routine, limited to three or four examinations during the six weeks following defervescence. An extremely interesting feature is the large proportion of cases in which a prolonged excretion of typhoid bacilli by the urine took place in addition to the more common and better known form of excretion by the fæces. As a rule, however, the bacilluria ceased spontaneously after a time (without the aid of urotropin, which in Semple and Greig's experience proved of little or no value as an inhibiting agent), while the fæces remained either continuously or intermittently infective. These tables are too lengthy for reproduction here, but the following summary may be of interest :

Case 1.	Defervescence	8 June, 1907.	Bacilluria ceased 1 Oct., 1907. Faeces positive on 25 Nov., ,,
Case 2.	,,	26 June, ,,	Bacilluria ceased 30 Aug., ,, Faeces always negative.
Case 3.	,,	8 July, ,,	Bacilluria ceased 8 Sept., ,, Faeces positive 21 Oct., ,,
Case 4.	,,	14 May, ,,	Bacilluria ceased 24 July, ,, Faeces always negative.
Case 5.	,,	22 Aug., ,,	Bacilluria ceased 2 Oct., ,, Faeces positive 8 Nov., ,,
Case 6.	,,	22 May, ,,	Bacilluria ceased 2 Sept., ,, Faeces positive 10 Sept., ,,
Case 7.	,,	17 Aug., ,,	Bacilluria ceased 16 Sept., ,, Faeces positive 10 Nov., ,,
Case 8.	,,	21 Aug., ,,	Urine positive 12 Nov., ,, Faeces positive 12 Oct., ,,
Case 9.	,,	10 June, ,,	Urine positive, 29 Sept., ,, Faeces positive 15 Sept., ,,
Case 10.	,,	4 Sept., ,,	Bacilluria ceased 12 Sept., ,, Faeces positive 18 Nov., ,,
Case 11.	,,	30 June, ,,	Bacilluri ceased 17 Sept., ,, Faeces positive 28 Sept., ,, (? ceased)
Case 12.	,,	20 Sept., ,,	Bacilluria (? ceased 6 Oct.), ,, Faeces positive 15 Nov., ,,

The daily observation of these cases extended over a period of less than six months in each instance. It will be of interest to know from further reports what proportion of these intestinal carriers continued to excrete the typhoid bacillus indefinitely in their faeces, and whether a recrudescence of the bacilluria occurred at a later period.

In addition to this complete examination of convalescents, an examination was also made of nursing orderlies who had been in attendance on typhoid cases. Four of these were examined over a long period after they had finished their course and were about to return to their regiments. None of them ever suffered from enteric fever in a typical form. Two of the men, however, were found to be excreting typhoid bacilli in their faeces. Such cases (probably "transitory" carriers or so-called "acute" carriers of Klinger) are of great importance from the epidemiological point of view, and there is abundant evidence that a proportion of these may pass into the chronic stage.

In a more recent report on army carriers in India by Aldridge (1909) it is noted that of 190 men whose excreta were examined, six were found to be discharging the bacilli more than six months after defervescence, *i.e.*, 3·1 per cent. of the convalescents. These were all invalided to England, and further examinations in this country yielded positive results up to 8, 12, 16 and 18 months.

An extensive enquiry into an outbreak of enteric fever affecting the 71st regiment of infantry at the Saint-Brieuc garrison in Summer 1909, has yielded further evidence showing the enormous importance of the atypical and unrecognised cases. The outbreak has been reported fully in all its aspects, epidemiological, clinical and bacteriological by Billet, Le Bihan, &c. (1910). Briefly, the source of infection was stated to have been in all probability contaminated cider, but the chief interest of the enquiry at least in connexion with the subject of this chapter, centres round the bacteriological findings.

There were treated in hospital 142 cases, *viz.*: 33 very severe, 72 moderately severe, 37 benign, with a total mortality of 13 or 9 per cent.

Blood cultures were made in 74 cases during the first week of the disease with 57 positive results. Widal examinations were done in 43 cases about the end of the third week, with 40 positive results. The faeces were examined in 129 cases at the end of 35 days after entering hospital, with 15 positive results, *i.e.*, 11·6 per cent.

In addition, a careful clinical examination was made of all suspects in the regiment, who showed the slightest symptoms of indisposition, and a surprising proportion of these was found to give either positive Widal tests or typhoid bacilli in the faeces. The clinical histories of these atypical or ambulatory cases are of great interest as showing how insignificant the clinical manifestations of typhoid infection may be. Of 57 such cases examined, 14 only showed a rise of temperature lasting three to five days, seven lasting two days, while the majority (34) showed complete apyrexia. Some were out of sorts for several weeks while others returned to their normal condition after only a few days' indisposition. In eight cases, constipation was the only symptom, while in 15, headache, furred tongue and loss of appetite were the predominant symptoms. Diarrhœa rarely occurred alone, being generally accompanied by swelling of the spleen, and sometimes rose-spots.

Other symptoms complained of in individual cases were stiff neck, angina and "rheumatic" pains. The bacteriological results in these cases were as follows:—

Cultures were made of the blood of 39 suspects with seven positive results, also of 53 men, who lived in rooms where typhoid cases had been most numerous, with one positive result. The stools were examined in 64 atypical cases with 13 positive results, *i.e.*, 20·3 per cent., whereas the percentage of convalescent carriers was only 11·6 per cent. (*see* above). There is no record of repeated examinations having been made in these cases, but the results are sufficient to show the important part which unrecognised cases may play in the spread of enteric fever. As Semple and Greig had found in their investigations that nursing orderlies were particularly liable to act as transitory carriers, so also in this French garrison a large number (11·4 per cent.) of "Infirmiers" showing only ephemeral symptoms of the disease, were discharging typhoid bacilli in their stools. Also the conductor of the ambulance in which the typhoid cases were conveyed to hospital, gave a positive Widal reaction and positive stools, although he appeared to be an absolutely healthy individual.

Tsuzuki (1910) records the results of an enquiry into the question of convalescent carriers in a division of the Japanese Army. The circumstances which gave rise to the investigation will be found detailed in Chapter VI. The bacteriological part of the work appears to have been carried out with great thoroughness, the tests being made practically every day during convalescence. The result was that three out of 51 convalescents in hospital continued to discharge typhoid bacilli beyond the three month limit, *i.e.*, carrier percentage of 5·8.

Further, a large number of examinations was carried out on (1) persons known to have had enteric previously; (2) healthy persons belonging to a company in which a recent case of enteric had occurred; (3) persons occupied in the canteen. In all 5,109 examinations were made of 2,785 persons, with the following results:—

—	Known previous infection.	No known previous infection.	Total.
Number of persons examined ...	316	2,469	2,785
Number of carriers found ...	6	2	8
Percentage of carriers	1·89	0·08	0·28

The particulars with regard to the investigation of these 11 carriers are of interest, and I append the following brief notes:—

CONVALESCENTS OF 1908 WHO BECAME CARRIERS.

A. Fell ill 9th June, 1908. Fever lasted 21 days. Bacilli present in faeces with few intermissions up to 26th December, when he was discharged from service.

B. Fell ill 26th February, 1908. Faeces positive on 19th July, but further examinations up to 3rd October negative, when he was released from isolation.

C. Fell ill 21st September, 1907. Relapse on 13th January, 1908. Urine positive on 13th April, but further examinations up to 23rd June negative. Faeces negative. Released from isolation.

CARRIERS WHO CONTRACTED THEIR PRIMARY INFECTION IN 1907.

1. Fell ill 2nd September, 1907. Faeces positive on 17th April, 1908 and on every subsequent examination up to 17th October, 1908, when he was discharged from duty. The urine was also repeatedly positive up to this time.
2. Fell ill 2nd September, 1907. Urine found to be positive on 17th April, 1908 and on all subsequent occasions up to 17th October, 1908, when he was discharged from active service. The faeces were never positive. Urotropin had little or no effect.
3. Fell ill 17th July, 1907. Faeces positive on 8th June, 1908 and with slight intermissions up to 17th October, 1908, when he was discharged from duty. Urine never positive.
4. Fell ill 30th November, 1907. Faeces and urine positive on 24th April, 1908. Examinations of faeces after 13th May were negative, but the urine continued positive till 23rd October 1908, when he was discharged from duty.
5. Fell ill 14th September, 1907. Faeces positive on 7th May, 1908, but all subsequent examinations up to 17th July were negative. Released from isolation.

6. Fell ill 28th August, 1907. Faeces positive on 19th April, 1908 and on subsequent occasions up to 30th June, 1908. Further samples in July, August, and September were negative. Released from isolation on 3rd October, 1908.

The remaining two carriers had never had definite clinical symptoms and might be called "symptomless" carriers. The one had been somewhat out of sorts in August, 1908 but quite fit for duty. On 2nd September he had given a positive Widal reaction (1 in 50), and examination of the faeces was positive up to 30th November, when he was discharged from service.

The other had absolutely no symptoms. He gave a negative Widal reaction and the faeces were found positive on two occasions only, viz., 11th July and 13th July, 1908. On 11th September he was released from isolation.

In America some valuable statistics have been collated by Rosenau, Lumsden, and Kastle (1909) and by Park (1908). The former investigated the question as to how far chronic carriers were responsible for the spread of fever in the district of Columbia.

Three series of examinations were performed.

1. Persons who had had enteric fever in previous years (6 months—20 years previously), and who had been in association with recent cases during 30 days prior to onset.

   Thirty-two such persons were examined with negative results.
2. In the course of enteric studies in special districts, the faeces of 71 persons who had had typhoid fever 1–10 years previously were examined, but all were negative.
3. In order to determine how many persons in Washington during the typhoid season were carriers, they examined from July 16th to November 8th 1,014 samples of faeces, and 26 samples of urine from 993 persons living in 32 blocks of the city.

   Out of this large material they found only three persons carrying the bacillus who did not present any clinical symptoms of typhoid fever.

The first was a male of 50 years who had never had typhoid fever. His wife had typhoid fever 38 years ago. There had been no typhoid fever in any house where he had resided, and he had enjoyed good health all his life. Some six weeks before, he had been out of sorts with a feeling of discomfort in the region of the liver (? typhoid cholecystitis). The bacilli were found only once and he gave a negative Widal reaction. It is unfortunate that no mention is made of the examination of his wife.

The second was a boy of 14 years. The bacilli were got on one occasion only. No one in the family had had typhoid fever except the boy's mother who had an attack 42 years ago. Here also no mention is made of the examination of the mother.

The third was a boy of nine years. The bacilli were found once only in the urine, while the faeces were negative. None of the family had ever had enteric fever, and these were all examined with negative results.

The percentage found (viz., 0·3 per cent.) accords well with that got by other observers in groups of healthy people associated or not associated with typhoid cases. Thus Minelli (1906) instituted a search for carriers in an institution which had been for years free of typhoid. He chose the town prison of Strassburg containing 250 inmates. The excreta of all these were examined with the result that one carrier was discovered. He had been eight weeks in the prison, and asserted that he had never been ill. His serum gave a high Widal reaction (1 in 1,000)—a fact which strengthened Minelli in his belief that the man may previously have had a slight attack of typhoid. He was 37 years old, and, being a vagabond, he may not unlikely have come in contact with typhoid cases.

Minelli's percentage was, therefore, 0·4.

Park (1908) examined in May and June, 1908, the stools of 52 persons who had had typhoid fever during an epidemic at a lunatic asylum eight months previously. Two were still discharging typhoid bacilli.

He also examined the faeces of 16 persons who had had typhoid fever at another asylum (date not given) and found two of these still positive. They had been well for six months. From this small series therefore he obtained a carrier percentage of six per cent. A large number of convalescents (number not given) were examined on leaving hospital when five per cent. were found to be still excreting typhoid bacilli.

I shall close these data gathered by individual observers with the recent report by Prigge (1909) on the carrier statistics at the Saarbrücken institute.

During the last three years they examined at that institute a total of 10,841 persons and discovered 84 carriers which are classed simply into two groups, (1) Temporary carriers who discharge bacilli up to one year, and (2) Chronic carriers who discharge for a longer period than one year.

It appears to me there are good grounds for extending, as Prigge does, the time limit from three months to one year in the case of temporary carriers, as doubtless, even admitting the difficulty entailed by intermittency, a considerable proportion of convalescent carriers who have passed the three-month limit may cease to discharge spontaneously long before a year has elapsed and therefore do not deserve the appellation "chronic" in the ordinary sense of that term.

In the first group he classes—

(*a*) Persons in whom the bacillus was found before clinical symptoms arose, *i.e.*, Primary carriers (Conradi) or Porteurs précoces (Sacquepée).

Three such carriers were discovered in whom the symptoms did not supervene till 18, 19 and 20 days afterwards. Two of these cases were children and the third was an adult man.

(*b*) Clinically cured persons who continue to discharge bacilli from ten weeks to one year after the attack.

There were 25 of these, viz., 9 men and 16 women.

(*c*) Healthy persons, 24 (16 men and 8 women).

In the second group he classes—

(*a*) Persons who have previously had enteric fever, 27 cases. The proportion of females to males in this small series Prigge does not state, but he notes that in a larger series of 102 cases taken from the whole campaign district, 17 were males and 85 females, thus showing the enormous preponderance of female chronic carriers.

(*b*) Persons who have never had typhoid fever, 8 cases, all women.

The difficulty of obtaining accurate past histories in these cases is, as other observers have found, very considerable, and there is little doubt that some at least of these cases may have had enteric fever in a slight or atypical form.

I come now to consider the carrier statistics compiled for the whole campaign district of South-West Germany from the commencement of the campaign up to the end of the year 1907. These have been recently very fully worked out and commented upon by Klinger (1909), now of the Kaiser-Wilhelms Academie in Berlin. The population of the district (excluding the Bavarian Pfalz) was at 1st December, 1905, about 2,300,000, distributed in 2,532 Gemeinwesen (communities).

Up to the close of 1907, 431 notifications of transitory and chronic typhoid carriers were made (three months being taken as the upper limit for a transitory carrier). These are arranged in the annexed table (reproduced from Klinger's report) according to age and the occurrence or non-occurrence of a definite primary infection.

TABLE I.

Age-Groups.	Chronic Carriers.						Transitory Carriers.					
	Previous Typhoid.			No Previous Typhoid.			Previous Typhoid.			No Previous Typhoid.		
	M.	F.	Total.	M.	F.	Total.	M.	F.	Total.	M.	F.	Total.
0–2 ...	—	—	—	—	—	—	1	3	4	3	2	5
2–5 ...	1	—	1	1	—	1	1	2	3	4	6	10
5–10 ...	1	2	3	—	1	1	4	9	13	11	11	22
10–15 ...	—	1	1	—	2	2	3	2	5	8	5	13
15–20 ...	2	4	6	—	—	—	2	11	13	4	10	14
20–25 ...	4	4	8	—	3	3	9	5	14	2	3	5
25–30 ...	1	13	14	1	3	4	2	6	8	7	5	12
30–35 ...	2	21	23	1	2	3	—	3	3	2	4	6
35–40 ...	3	18	21	—	6	6	2	9	11	6	1	7
40–45 ...	6	21	27	—	3	3	1	6	7	3	2	5

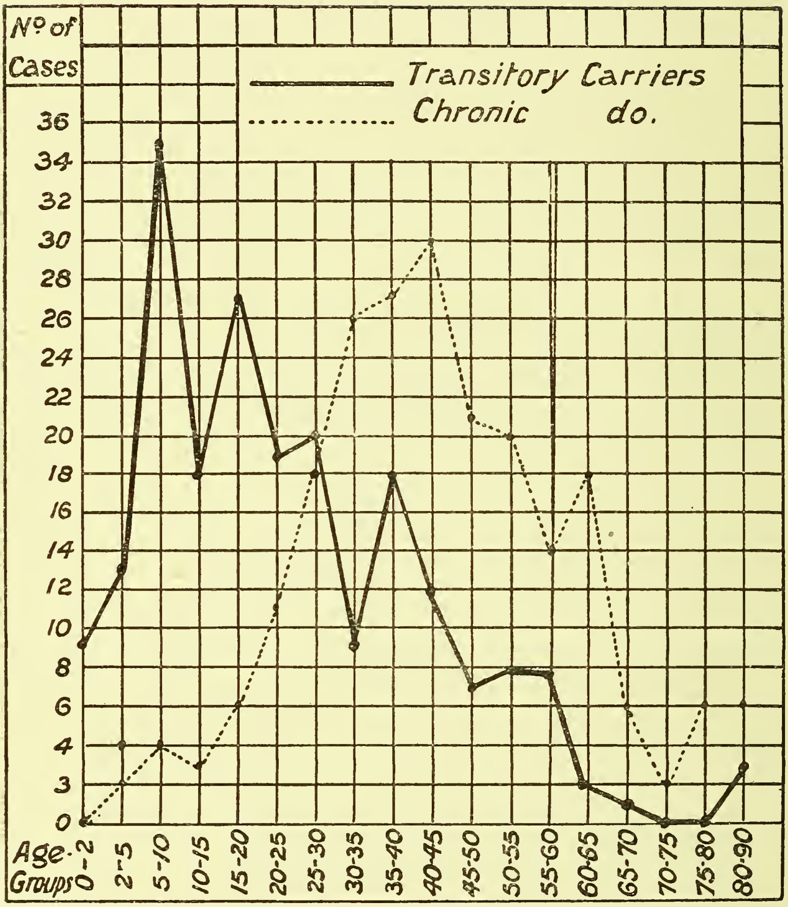
Nº of Cases
Transitory Carriers
Chronic do.
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
3
0
Age-Groups
0-2
2-5
5-10
10-15
15-20
20-25
25-30
30-35
35-40
40-45
45-50
50-55
55-60
60-65
65-70
70-75
75-80
80-90

TABLE I.—*continued.*

Age Groups.	Chronic Carriers.						Transitory Carriers.					
	Previous Typhoid.			No previous Typhoid.			Previous Typhoid.			No previous Typhoid.		
	M.	F.	Total.	M.	F.	Total.	M.	F.	Total.	M.	F.	Total.
45–50 ...	1	18	19	—	2	2	—	1	1	2	4	6
50–55 ...	4	12	16	1	3	4	2	1	3	2	3	5
55–60 ...	1	7	8	—	6	6	3	3	6	1	1	2
60–65 ...	2	13	15	1	2	3	—	—	—	1	1	2
65–70 ...	2	3	5	—	1	1	—	—	—	1	—	1
70–75 ...	—	—	—	—	2	2	—	—	—	—	—	—
75–80 ...	2	3	5	—	1	1	—	—	—	—	—	—
80–85 ...	1	1	2	—	—	—	—	—	—	—	1	1
? ...	—	2	2	—	2	2	1	—	1	1	2	3
Totals ...	33	143	176	5	39	44	31	61	92	58	61	119

There were thus 220 chronic carriers and 211 transitory carriers. Of the former the great majority (80 per cent.) gave evidence of a primary infection, while in only 43·6 per cent. of the transitory carriers was this evidence forthcoming.

The enormous preponderance of female chronic carriers over male is strikingly brought out (viz., 182 to 38, or nearly 5 to 1), whereas among the transitory carriers the proportions are very nearly equal (female to male, 1·4 to 1).

Gallstone troubles were definitely diagnosed in 30 chronic carriers, *i.e.*, 13·6 per cent. This figure corresponds closely to the percentage of gallstone cases (of all origins) in which diagnostic symptoms are present.

Perhaps the most important and striking feature brought out by the Table is the different distribution of the transitory from that of the chronic carriers according to age groups. Whereas among the transitory carriers young persons form the great majority, among the chronic carriers persons in middle age or advanced life predominate markedly.

This is shown more clearly in the annexed curve in which the maximum point for the transitory carrier is reached at the 5–10 age limit and that for the chronic carrier at the 40–45 age limit. It is important to note, however, that the curves indicate only the actual incidence on the several age-groups and not the proportional incidence.

With regard to the period during which these carriers have been under bacteriological control since they passed the three-month limit, 30 have been examined up to six months and the others from one year to two, three, four and four-and-a-half years.

Included in the 220 chronic carriers are some 30 cases in which the primary infection took place 4–30 years previously.

A spontaneous cessation in the excretion of the typhoid bacillus occurred in 42 of these chronic carriers, sometimes indeed after prolonged positive periods, but as Klinger remarks, such bacteriological cures must be regarded with considerable scepticism in view of the prolonged intermittent periods which have been observed and the not unlikely possibility of the transmission of a false sample.

During 1906 and 1907, 38 typhoid convalescents or 1 per cent. of the total number of typhoid cases (3,867) became chronic carriers. The percentage is thus much smaller than that obtained by individual observers.

Further facts with regard to the campaign particularly during the earlier years 1904, 1905 and 1906 are given by Frosch (1908). There was a total of 6,708 enteric cases in that period (beginning of 1904–end of 1906), and of these 310 became carriers; 166 excreted the bacillus for three months or longer, *i.e.*, 2·47 per cent. (= Dauerträger) and 144 excreted the bacillus for a period under three months, *i.e.*, 2·15 per cent. of transitory carriers (= Bazillenträger).

In Frosch's series females again formed 82 per cent. of the chronic carriers and 60 per cent. of the transitory carriers, while children (up to 15 years) formed only 4 per cent. of the chronic carriers, but 35 per cent. of the transitory carriers.

An interesting point with regard to the occupations of the female typhoid cases, is brought out from Frosch's figures. For the year 1906, the total number of typhoid cases in the district was 2,080 (938 males, 454 females, and 688 children up to 15 years). Of these 454 females no fewer than 314 were "Hausfrauen," while 56 were domestic servants. Thus 370 or 81 per cent. of the female cases were engaged in housework, and from these the great majority of the chronic carriers and more than half of the transitory carriers were recruited.

I shall deal with the significance of this fact when I come to consider the pathogenesis of the carrier state (*vide* Chapter VII).

The data for the Bavarian Pfalz have been compiled by G. Mayer (1910).

In July, 1903, Bavaria decided to join in the campaign that had been begun in the neighbouring districts of south-west Germany and erected two institutes at Landau and Kaisersläutern respectively. G. Mayer directed the latter up to 1st February, 1908. The population of his district was about 400,000 and the number of typhoid cases was about 930 during the period (1904–1907).

Typhoid carriers to the number of 151 were found, viz., temporary (under three months) 73, chronic (over three months) 78. Of the temporary carriers 54·9 per cent. were women and 57·4 per cent.

children, while of the chronic carriers 65·5 per cent. were women and 25·2 per cent. children (up to 15 years).

Nine of the chronic carriers (or roughly 10 per cent.) suffered from gallstone trouble, while three had severe "bilious" relapses after three, six and ten years respectively.

According to the carriers' own statements, 16 of them had never been ill, 10 had had enteric fever four–nine years previously, and two of them had had enteric fever 20–30 years previously.

"Bacteriological" cures resulted in 62 chronic carriers, four left the Pfalz district and one (a servant girl) drowned herself.

The great majority of the carriers dealt with in this chapter are adult males and females of the chronic type. The records show that children only very rarely become chronic carriers, but their importance as temporary carriers has been repeatedly proved since bacteriological methods have shown how insignificant and how liable to be overlooked a typhoid infection may be in young children.

I do not propose to give actual instances in illustration of the spread of infection by transitory carriers in the persons of young children, but I cannot refrain from quoting one striking case in which a series of typhoid cases was considered to be due to a suckling male child of 18 months. This case has quite recently been reported by Rommeler (1910) of the Neunkirchen Institute. The facts are as follows :—

On 29th November, 1909, a woman who was suckling a child of 18 months developed vague febrile symptoms. Eight days later she was removed to hospital where she passed through a typical attack of enteric fever. Up to the time of her removal to hospital she continued to nurse the child. The latter was then handed over to a female neighbour to be nursed. On the first day of her custody (viz., 8th December, 1909) she noticed that the child had slight diarrhœa, but which she not unnaturally attributed to the necessary weaning.

On 25th December the *foster-mother* developed typhoid fever. On 4th January, 1910, her *six-year old daughter*; on 6th January her *three-year old niece*, who came every day to play in the house; on 18th January her own *suckling child*, and on the same date her *fifteen-year old daughter* fell ill with the same disease. As almost the whole family was attacked, a relative (female of 20 years with some experience in nursing) was called in to take care of the sick. She also took ill on 2nd February and died in six days.

There appeared to be little doubt that the series of cases arose from the suckling child temporarily adopted by the family, but the suspicion was raised to a certainty by the result of the bacteriological examination carried out. On 19th January, 1910, the serum of the child gave a Widal reaction of 1 in 100. Also on two occasions, 21st and 25th January, typhoid bacilli were isolated from the child's faeces, but nine subsequent examinations were negative.

The importance of the atypical and ambulant cases in children is further exemplified in a recent paper by Brückner (1910–*b*).

I close this chapter with some data relative to the so-called "Primary" or "Precocious" carriers in whom typhoid bacilli have been demonstrated in the excreta some time before the outbreak of symptoms. G. Mayer (1910) in a recent paper states that in 1903 he was the first to demonstrate the presence of typhoid bacilli in the stools during the incubation stage. The case was a boy of six years whose stools contained typhoid bacilli eight days before symptoms arose. Although he was immediately isolated, both his brothers contracted the fever. In 1905 and 1907 the same author was able to record two further cases of this nature.

Conradi (1907*b*) gives notes of two cases in which the bacilli were found in the faeces during the incubation stage.

Case I.—Typhoid fever broke out (9th to 18th April, 1906) in a family of eight members, the persons attacked being the mother and three children. On 20th April the cases were brought to hospital, having been nursed up to that date by the grandmother (61 years of age). Typhoid bacilli were isolated from the grandmother's faeces on 2nd May, 1906, and eight days later she also developed typhoid fever.

Case II.—On 27th December, 1903, a man 30 years of age fell ill with typhoid fever and was nursed by his wife till 10th January, 1904, when he was removed to hospital. On 25th January, 1904, typhoid bacilli were found in the healthy woman's faeces and eleven days later she also developed typhoid fever.

The importance of these cases and the infections arising from them (so-called early contacts) have been for some years strongly insisted upon by Conradi who was also able to demonstrate the presence of typhoid bacilli in the blood during the incubation stage. In the beginning of March, 1907, a girl contracted enteric fever. On the 24th March Conradi took a sample of blood from her brother who was at the time quite well and isolated the B. typhosus therefrom. Four days later this boy also fell ill with typhoid fever of a severe type.

I cannot enter in detail into the statistics which have been compiled, notably by Conradi (1907*c*) and Klinger (1909) on this "early contact" question, but I extract from their works the following tables which, it is claimed, show the relatively high infectivity of typhoid patients during the incubation stage and the earlier weeks of the disease.

The material at Conradi's disposal for the investigation of this question was derived from the data relative to certain groups of cases carefully selected from the total of 600 cases investigated during a period of 2½ years, at Saarbrücken. In calculating the date on which the primary case infected the secondary, he took the interval between the beginning of the primary case and the beginning of the secondary and subtracted therefrom 10 days.

In Table I. are recorded the data relative to 38 contact infections (secondary cases) which took place in various families in spite of the fact that the respective primary cases had been removed to hospital. As a rule 12 days elapsed between the beginning of the disease and the removal to hospital. On the day after removal the house was thoroughly disinfected. Conradi considers that the table shows that the great majority of the secondary cases must have received their infection from the primary cases, while the latter were still in the early days of their illness.

In Table II. are given the data with regard to a series of secondary cases which arose in families in spite of disinfection and isolation of the primary case in the house. Satisfactory isolation was admittedly difficult in many cases, so that there may have been some opportunity of infection after the 12th day, when disinfection was, as a rule, performed.

In Table III. are given the data relative to secondary cases due to primary cases not treated by a physician.

TABLE I. (CONRADI, 1907*c*).

Data relative to 38 contact infections which took place in various families in spite of the fact that the first person attacked was removed to hospital.

Infected by the primary case during the	1st	week of the disease,	25	secondary cases.
" " "	2nd	" "	7	"
" " "	3rd	" "	4	"
" " "	4th	" "	1	"
" " "	5th	" "	1	"

TABLE II. (CONRADI, 1907*c*).

Data relative to 28 contact infections which took place in families in spite of disinfection and isolation of the primary patient in the house.

Infected by the primary case during the	1st	week of the disease,	14	secondary cases.
" " "	2nd	" "	7	"
" " "	3rd	" "	2	"
" " "	4th	" "	2	"
" " "	5th	" "	1	"
" " "	6th	" "	1	"
" " "	7th	" "	1	"

TABLE III. (Conradi, 1907c).

Data relative to 19 contact infections due to typhoid cases not treated by a physician.

Infected by the primary case during	1st	week of the disease,	10	secondary cases
" " "	2nd	" "	2	"
" " "	3rd	" "	4	"
" " "	4th	" "	2	"
" " "	5th	" "	1	"

These 85 contact infections may be thus summarised, 10 days being taken as the most probable incubation period.

Infected by the primary case in the	1st	week of the disease,	49	secondary cases.
" " "	2nd	" "	16	"
" " "	3rd	" "	10	"
" " "	4th	" "	5	"
" " "	5th	" "	3	"
" " "	6th	" "	1	"
" " "	7th	" "	1	"

It will be seen that 58 per cent. of the observed contact infections took place during the first week of the primary infection, and in view of the facts that have been ascertained with regard to the infectivity of the incubation stage, Conradi considered it probable that a considerable proportion of these may have become infected during the incubation stage of the primary case.

The table compiled by Klinger (1909) from the data relative to the two years 1906 and 1907 of the typhoid-campaign in south-west Germany, affords a striking illustration of the importance of the primary carrier, in the spread of enteric fever.

The material employed was a series of 812 contact infections, two weeks being taken as the average incubation period. In 60 cases Klinger believed that he had ascertained the incubation period with tolerable certainty ; he found it to vary from 5 to 45 days, with an average of 16 days. Also in the course of a water-borne epidemic he had found that 98 per cent. of a series of 83 cases regarded as having been infected at the same time developed clinical symptoms 11 to 18 days later.

(Klinger, 1909).

Incubation Period.		Course of the Disease.			
1st week.	2nd week.	1st week.	2nd week.	3rd week.	4th week.
(1906) (1907) 18 + 15	84 + 66	104 + 83	87 + 71	58 + 58	16 + 43
33 contact cases.	150 contact cases.	187 contact cases.	158 contact cases.	116 contact cases.	59 contact cases.

Course of the Disease.					
5th week.	6th week.	7th week.	8th week.	9th week.	10th week.
13 + 21	7 + 15	9 + 5	9 + 7	10 + 5	5 + 3
34 contact cases.	22 contact cases.	14 contact cases.	16 contact cases.	15 contact cases.	8 contact cases.

Klinger admits it would be a mistake to place too much reliance on the accuracy of the figures in view of the variations in the incubation period ; nevertheless he takes the view that taken as a whole the figures show that a preponderant number of contact infections take place during the early period of the typhoid infection, or, in other words, that a typhoid patient is most dangerous during the incubation period, and the first and second weeks of the disease, *i.e.*, during the period when little or no precautions can be taken. In the later stages of the disease the gradual cessation in the excretion of the specific bacteria and the precautions taken as to disinfection, &c., serve to keep the contact infections at a relatively low figure.

CHAPTER III.

Instances of Infectivity of Carriers.

House and Street Cases.

The influence of carriers in maintaining the endemicity of typhoid fever in individual houses and streets, or groups of houses in isolated country districts, has been abundantly attested by the work of recent years, and in no other sphere has the search for carriers been more fruitful. Indeed, so many instances of the dangers arising from carriers in this connexion have accumulated that it will be possible to refer in detail only to the most striking and illustrative. The part played by carriers in the dissemination of enteric fever through the agency of milk or of water and their relationship to the occurrence of the fever in army-units and in institutions will be discussed in following chapters.

I shall commence with the now well-known case of the Strassburg baker's wife, reported four years ago by Kayser (1906*a*).

On 20th May, 1904, an apprentice, lodging with the master baker's wife, a woman 40 years of age, contracted typhoid fever and died during the third week of the disease. The baker's wife was known to have had typhoid fever ten years previously. In recent years it had been observed that practically every fresh apprentice became ill shortly after his entering on residence with her, with symptoms pointing to stomach and bowel disorder. These symptoms were attributed by the baker's wife to "too good diet." On 26th May, 1904, this woman was discovered to be a carrier, and further examination of her stools on 1st June, 3rd June, 22nd June, and 5th July proved positive. From the 19th July onwards, however, weekly examinations of her stools gave negative results; but there was a strong conviction that the samples received from her were not her own.

On 8th August her tenant, a man 29 years of age, who used the same water-closet as the baker's wife took ill and died in the third week of the disease. Under police pressure the woman was now brought to the clinic and her stools were found to contain enormous numbers of typhoid bacilli.

In a later communication Kayser (1907) attributes another case of typhoid fever to infection from the baker's wife.

Thus three cases occurred in the household of this woman.

Second case. Kayser (1906*a*).—A female 40 years of age was discovered to be a carrier in November, 1904, and her stools and urine were examined every three weeks thereafter for about a year. Thirty years previously she had passed through an attack of typhoid fever, and during the past five years she had suffered from severe gallstone colic.

On 20th May, 1904, her son-in-law (27 years) who lived in the same house, fell ill with typhoid fever, as also, on 17th November, did her lodger, who succumbed to the disease. These two persons had used the same water-closet and the same dishes, &c., as this woman. Two other persons, who did not belong to the household, but who came in contact with the woman in a business capacity, also contracted typhoid fever. After the 20th November, 1904, when she was discovered to be a carrier and regulations as to disinfection, &c., were in consequence imposed upon her, no further cases occurred in her vicinity. No record could be obtained of the occurrence of cases in this household prior to 1904.

A number of interesting cases of household infections traceable to carriers are given by Mayer (1908) in his report on the typhoid investigations in the Bavarian Pfalz during 1903–6.

Case 1.—In August, 1906, a girl (13 years) in the hamlet of " V " was notified as a case of typhoid fever. One death from typhoid fever had occurred in this hamlet on the 14th April, but no connexion could be traced between this and the August case. It was ascertained, however, that the grandmother of the girl had had typhoid fever 49 years previously, her grandfather 20 years previously, an aunt 28 years previously, her mother 23 years previously, and a brother 9 years previously. In the course of an examination of these persons, the mother (41 years) was found to be a carrier.

Case 2.—A young married woman was notified in April, 1904, as a case of typhoid fever, and the medical officer stated that her eighteen month's old child had suffered from angina and diarrhœa about 14 days before the commencement of her mother's illness. Where the woman lived there had been only one case of typhoid fever in recent years, but no connexion could be traced between this case and the sick family. The case would have remained puzzling without a knowledge of other cases which had occurred in earlier years in this place. On consulting the registers Mayer found a patient who had had typhoid fever in 1900, and whose name was the same as that of the sick woman. Enquiry established the fact that this man was the husband of the sick woman and the father of the child, and further examination led to the discovery that he was a carrier.

Case 3.—Typhoid fever had been endemic on a large estate in " L " since 1896. Soil contamination had been blamed, but in spite of improved drainage cases continued to crop up. Repeated disinfection of the rooms in which typhoid cases had occurred also failed to arrest the spread. Cases had arisen in the following order :—

1896. The manager himself, and, later in the same year, a girl employed at the farm.
1897. The housekeeper.
1899. A girl, in middle of July, employed on the farm.
1900. Ditto ditto ditto.
1903. Ditto ditto ditto.
1897–8. Three persons in a neighbouring house, where relations of the manager resided.
1900. A labourer living in a house exactly opposite the farm.
1901. A farm labourer and his master, who died.
1902. Two other farm labourers, one of whom died; also a girl in a neigbouring house.

In June, 1906, four persons living in three houses not far from the farm took typhoid fever. Their water supply—a rather unsatisfactory pump-well—was the same as that of the farm and there was a suspicion that it was being polluted from a water-closet employed by the manager of the farm, and, in fact, 14 days before the outbreak of the new cases the manager had been known to use this closet. His faeces were now examined and he was discovered to be a carrier. It was practically certain that for years he had been spreading typhoid fever in his vicinity.

Rosenthal (1906) in Göttingen gives an interesting description of repeated cases in one household attributable to a carrier.

During the autumn and winter of 1905–6 there had been four cases of typhoid fever in a single household and the faeces of 13 inhabitants of this house were examined, with the result that one female carrier (42 years) was discovered. She had not been ill for years but there was some evidence of her having passed through an attack of typhoid fever in 1878. In that year she had had a severe febrile attack and at the same time her son had a severe intestinal trouble. During that year also an epidemic of typhoid fever had broken out in her street. On enquiry it was found that from 1897 to 1906 13 cases of typhoid fever were in all likelihood attributable to personal intercourse with this woman. Six of these persons were lodgers who got breakfast and supper from her; three were children who lived in the house; one was a female neighbour, who often visited her; and three were persons in neighbouring houses who got their vegetables from her. This woman and her husband sold vegetables and fruit and attended the markets three times a week. She may therefore have infected many more people. Rosenthal also notes that the excreta from the house were used to dung the vegetables. Necessary precautions were now enforced with regard to disinfection of excreta, but there was no power to prevent the woman plying her trade.

Mention may now be made of a well-known case reported by Soper (1907) of New York, in which a female carrier in the person of a cook was found to have been responsible for the occurrence of no fewer than 26 cases of typhoid fever in seven different families.

The final outbreak attributable to this cook occurred in the first two months of 1907 while she was in service in a New York family, the victims being a chambermaid and a daughter of the house, who died (the only fatal case in the series). The cook had been two months in this family before the cases arose. On March 19th, 1907, this woman, after a severe struggle in which police aid had to be requisitioned, was conveyed to the detention hospital, under charge of Drs. Wilson and Park, and there, her faeces were bacteriologically examined with a positive result. Much difficulty was experienced in tracing out the past history of this cook and possibly the achievements now to be mentioned have no claim to be exhaustive. Considerable gaps in her history could not be filled up in spite of careful enquiry.

The various outbreaks occurred as follows:—

September, 1900. Mamaroneck. During a summer residence in this place a visitor to the family developed typhoid fever. It is remarkable that the cook had been three years in this family without having given rise so far as is known to any case of the disease.

December, 1901. New York. One month after the cook's arrival in this family a laundress in their employment developed typhoid fever.

Summer, 1902. Dark Harbour. Seven members of the family and two servants developed typhoid fever. All the servants except the cook had been employed in this family for one month or more in New York before leaving for the summer residence in Dark Harbour. The cook had been engaged specially for the summer, and had joined the family three weeks before it left for Dark Harbour.

Summer, 1904. Sands Point. Four servants developed typhoid fever. The cook had been nine months in the service of the family without any untoward occurrence. The cases arose when the family removed to Sands Point, and the servants were practically new hands. (Laundress, gardener, butler's wife, and butler's wife's sister.)

Summer, 1906. Oyster Bay. Six cases occurred in one household.

September to October, 1906. Tuxedo. One laundress took ill 14 days after the arrival of the cook.

January to February, 1907. Final outbreak at New York (already quoted).

In a further report on this case Park (1908) mentions that the cook had been kept in detention since she was discovered to be a carrier, and that various intestinal antiseptics had been employed with a view to cure, but without success. Her urine was always negative.

Niven (Medical Officer of Health, Manchester) (1908), reported the discovery of a carrier in the person of a woman who kept lodgers and did her own housework. The cases ascribed to her occurred as follows :

September 24th, 1908. Male lodger (36 years) developed enteric fever four days after leaving the house.

September 7th, 1907. Male lodger (19 years) developed typhoid fever.

September 4th, 1906. Male lodger (28 years) took typhoid fever and died.

May 2nd, 1906. Male lodger (28 years) took typhoid fever and died.

The following three cases were also traced to two other houses at which Mrs. W. had taken in lodgers :—

May 20th, 1905. Lodger (19 years). This case, however, may have been infected outside Manchester.

April 8th, 1905. Lodger (25 years) developed typhoid fever.

October 4th, 1898. Lodger (23 years) took typhoid fever and died.

In none of these cases was there a history of contact with actual typhoid patients, nor could shell-fish consumption be incriminated. The history of Mrs. W. was briefly as follows :

> Up to her 54th year she had been quite healthy. In this year (1893) she had an attack of influenza and pneumonia. The illness had lasted five weeks, and she had been kept on fluid food. Since this illness she suffered periodically from pain in the abdomen and vomiting. In 1898 the attacks were very numerous and occurred at intervals of three to seven days. This year was marked by the first appearance of typhoid fever among her lodgers.
>
> When the woman was examined in November, 1908, no abnormal physical signs could be made out, the liver was not enlarged and there was no palpable enlargement of the gall bladder. There was no evidence of gall stones, and so far as her own medical attendant knew, she had never been jaundiced.
>
> Examination of her excreta by Prof. Delépine on November 4th, 1908, revealed typhoid bacilli both in faeces and urine. On December 3rd, however, the faeces only contained the bacilli. In November, 1907, her blood had given a negative Widal reaction, but on November, 1908, a positive reaction was obtained.

An account of this case has also recently been given by Hutchinson (1910).

Gregg (1908) (America) reported that seven cases of enteric fever had occurred among the inmates of a small boarding house in a farming town between August, 1905, and March, 1908. The mistress, who prepared all the food herself, had had typhoid fever so long ago as 1856. The faeces of this woman were repeatedly positive, but the blood and urine were negative. She enjoyed excellent health. No other cases occurred in the neighbourhood, and there was no other discoverable source of infection.

Another house-endemic persisting over a long term of years and attributable to a female carrier, has been reported by Huggenberg (1908). Thirteen cases in all occurred in one family during the period 1877–1908, viz. :—

Mother : May, 1877.
Father : July, 1886.
Son : September, 1892.
Female servant : February, 1899.
Do. August, 1899.
Do. September, 1900.
Do. August, 1902.
Daughter-in-law : September, 1902 (had been living for some weeks in the family).
Female servant : February, 1903.
Do. October, 1903.
Do. December, 1904. (This servant was living in the same house but with another family.)
Do. June, 1905.
Do. February, 1908.

Huggenberg made a bacteriological examination of the excreta of all the members of the family and was able to demonstrate typhoid bacilli in those of the mother, who had had her primary attack of enteric fever 31 years before. Her serum also gave a well-marked Widal reaction.

A few new experiences have recently been reported by Kayser (1909) in the course of the investigations at Strassburg.

Case 1.—House case with evidence pointing to the mode of transference of the infective agent from the carrier to the new host.

Frau H. (31 years) had had typhoid fever in her youth. Until August, 1905, she had lived with her three children, aged 4, 7, and 10 years, in a sanitary dwelling, and there had been no cases of the fever. During this month the family removed to a new suburban building in which the water-closet arrangements were not satisfactory, and the well was insufficiently protected from risk of contamination by the excreta of the household. This well formed the household water supply and was not used by other households. The children drank of this well water. On 19th August the seven-year-old daughter fell ill with typhoid fever, as also did the 10-year-old son, who died. It was then discovered that the mother, who had had typhoid fever 14 years before, was a chronic carrier. Nothing had happened while the sanitary arrangements of the house were above suspicion.

Case 2.—Where the medium of transference was in all probability food stuffs.

Frau B. went to a neighbouring town to attend Frau J. in childbirth. Some of the latter's family had had typhoid fever three months before, but all of these during convalescence had been declared typhoid-free. On her return home from attendance on Frau J., Frau B. took with her some fruit and pastry of which she and her husband partook. The husband shortly afterwards developed typhoid fever, and Frau B. was for some days out of sorts, but there was no reason to suspect that her illness was typhoid fever. The household of J. was examined, and Frau J., who was quite well, was discovered to be a carrier.

Herr B. after his attack also became a chronic carrier and received instructions with regard to the disinfection of his excreta. After the middle of February, 1907, he neglected to take the prescribed precautions. In March, 1907, Frau B. had an accident to her abdomen followed by what was thought to be a traumatic perityphlitis, but which proved to be typhoid fever. In Kayser's view the trauma was probably a factor which predisposed to the contraction of the fever (*vide* Chap. XII.).

Case 3.—This case is also interesting as showing how important it is to see that the disinfection of excreta is properly carried out by persons who are found to be carriers.

A shoemaker's wife, Frau E. (50 years), was discovered to be a chronic carrier in September, 1905. In July, 1905, a daughter, and in August–September an adult, son of Frau E., had contracted typhoid fever. The woman objected to the disinfection of her stools and resented interference with her domestic arrangements. Near her house lived a young married daughter of hers who frequently visited her along with her child. The latter took ill in Septemder, 1905, and died, and the daughter herself took ill and died in June, 1906.

Brückner (1910) records another instance of a female carrier who refused to carry out her instructions. For some years she had been under observation as a carrier, but cases attributable to her continued to crop up from year to year, and in 1909 had reached the respectable total of 13, including one fatal case.

This woman decidedly refuses to carry out her instructions and will, therefore, remain a standing danger to the community.

An interesting account of endemic typhoid fever in a country district associated with a carrier case is given by Baumann (1908) of the Metz bacteriological station.

At the end of August, 1906, the station at Metz received notification from the station at Hagenau that a male typhoid patient, Michael M., in the hospital at "S," had probably contracted infection at a farm "G" in the Metz sphere of operations. It was ascertained that Michael M. was engaged only for a short time in the summer at "G," in the capacity of shepherd; that at dinner time only he visited the farm, and slept at night in the fields. At the farm there had been of late no cases or suspected cases of typhoid fever, but at a farm "R," situated half-a-kilometre from "G" a girl Amalie E. daughter of Leonard E., the tenant of the farms "G" and "R," had been suffering for some time from a throat affection. The shepherd had not visited this farm "R." Amalie E. (25 years) was found to have had an illness in "R" and was now recovering. From the symptoms alleged, it was impossible to exclude a diagnosis of typhoid fever. Specimens of her blood and stools had been sent by her physician to the station at Metz, but in spite of the negative report he believed the case to be one of typhoid fever. No notification was made. Baumann accordingly examined blood samples from Amalie E. and also from her sister Fanny E. (31 years), who cooked for the farm "G" where the shepherd had his meals. This girl Fanny affirmed that she had never suffered from typhoid fever or any similar complaint. Five years ago, however, she had been troubled for some time with constipation. In both cases the Widal test was positive. It was therefore tolerably certain that Amalie E., whose first Widal was negative and second positive, had passed through an attack of typhoid. Repeated examinations of the stools of both girls were negative. A sample from Josephine E., who also worked in the kitchen at "G," was negative.

On 28th August a blood sample was received from a day labourer, Magdalena E., living in the same parish, "J," who had been ill in June but had only now called in a physician. This specimen was positive, but her stools and urine were repeatedly negative. During the summer this woman was engaged at the farm belonging to Leonard E., where she also got her midday meal. In this case also it seemed probable that the illness had been typhoid fever.

In the village "J" itself there had been no typhoid cases for several years.

On 20th September, 1906, a day labourer, Anton S. (32 years), belonging to "J," and who also went to work at the farm "G," contracted typhoid fever. His Widal was positive but stools and urine were negative. (This man later infected his two year old daughter Octavia S. who contracted typhoid fever on 26th November, and had a positive Widal and typhoid bacilli in her stools).

Inquiry was now instituted at the farms " G " and " R " (separated by 3 kilometres). At " G " two new cases were found which had not been notified, viz., a son Albert E. (23 years) who took ill on 23rd September and a daughter Louise E. (27 years) who had been ill since 5th October (Widal positive).

A sample of blood was also taken at the same time from the father Leonard E., a very healthy person. It was negative. However, both from him and the other members of the family stool and urine samples were taken. In Leonard E.'s stool the bacillus typhosus was found on 23rd October, but as his stool arrived on the same day as those of the sick members of the family, a suspicion arose that the samples had got mixed. Repeated examination, however, of the stools of Leonard E. proved positive, and there was no doubt that he was a chronic carrier. For several years this man had suffered from gallstone colic.

Further enquiry showed that in the autumn of 1905 in a neighbouring village " W," three persons had been ill with typhoid fever, two of whom worked at the farm " G." The third was the daughter of one of these labourers. In all these cases the Widal test had been positive, one of them had the B. typhosus in the urine and in another both stools and urine contained the bacilli.

Alfons M., brother of Michael M., went as shepherd to the farm " G " in his sick brother's place. He also took typhoid fever (Widal positive. Stools positive). On 16th October three new cases were notified, viz., two members of the family E., living at the farm " G," and a case in the village " M," situated about 5 kilometres from " G." This latter was a five-year-old boy who had been for some time on a visit to his grandfather Leonard E. at " G." It was further ascertained that a brother of this boy (7 years) had had typhoid fever in July and died on 1st August. He also had previously been on a visit to his grandfather Leonard E. The two cases at the farm " G " were a son, Emil E. (19 years) and the servant girl Josephine E. (16 years).

No further cases occurred in the neighbourhood for some months, but on 19th March, 1907, another case in " J " was notified. This was a day labourer (stool and urine positive). On 25th March two further cases were notified from the neighbouring village of " L." These were two farm labourers (23 years and 25 years). Another case was found to be convalescing but gave a positive Widal.

All the four cases just mentioned had been employed intermittently at the farm " G " as day labourers.

Further cases had not occurred in this locality up to the time of writing.

Thus 16 bacteriologically proved cases of typhoid fever in all likelihood derived their infection directly or indirectly from Leonard E.

Baumann states that besides these 16 cases, there had undoubtedly been numerous slight infections not recognised as typhoid fever and where no physician had been called in.

The part played by carriers in maintaining the endemicity of enteric fever in country districts is further exemplified by the four cases reported by Watt, Medical Officer of Health, Aberdeenshire, 1909, in his report on the health of the County for the year 1908. My thanks are due to Dr. Watt for kindly supplying me with additional data. One of the four cases will be described in detail in Chapter IV. The histories of the other three cases are briefly as follows :—

Case 1.—A female carrier (aged 65 years) was discovered in connexion with a case of enteric fever on a farm "S" in Aberdeenshire in August, 1908. The person attacked was the farmer, who died, and the carrier was his housekeeper. This woman had had enteric fever in 1900 while a patient in a lunatic asylum (*see* account of carrier-cases in this asylum, Chapter V.). Soon after her recovery from the fever, which was a severe one, she was discharged from the asylum and went to reside at a farm "B" for a short time. At this farm an outbreak occurred and it was ascertained that this woman had been living at the farm when the first case occurred there. Subsequent outbreaks occurred in places where she was employed as cook or cook-housekeeper. Hotel in "R," 1901, October, three cases. Farm "A," 1902, April, three cases.

Also at another house where she was in service during 1902, the master and his daughter were attacked by an illness which in the light of subsequent events may be regarded as having possibly been typhoid fever, though not diagnosed as such.

Farm "O," 1905, January, two cases. Farmer and his son.

Farm "F," 1907, August, two cases. Male servants.

It is interesting to note that in view of the danger arising to the community from this woman, the Local Authority, with the consent of the Local Government Board for Scotland, resolved to grant her an allowance of five shillings a week until she reached the age when she would be entitled to a pension, on condition that she did not engage in any work involving the handling of food. This offer was accepted.

Case 2.—This female carrier (aged 43 years) was discovered in connexion with an outbreak of typhoid fever at a farm, involving three people, viz., two male servants and one female servant.

The daughter of the carrier was also attacked. A sister-in-law of the carrier (who was the farmer's wife) was living in the neighbourhood as a summer visitor and getting milk from her farm. She, too, with her two daughters developed enteric fever on their return to Aberdeen.

There had been previous outbreaks at this farm in 1892, 1897 and 1906. It was in 1890 that the farmer's wife had her primary attack just before her marriage. She and her husband took the farm in 1892 and the first outbreak occurred in that year, when the persons attacked were (1) the husband, aged 28 ; (2) a child, aged 13 months ; (3) a brother of the farmer who assisted with the farm work. There had been no previous cases at this farm.

In 1897 a man-servant and in 1906 a child of nine months were notified as cases of typhoid fever. Other illnesses had, however, occurred in the family, and these the medical attendant is now inclined to regard as having been probably typhoid fever.

Case 3.—This female carrier (aged 28 years) was the wife of a cottar on a farm. She had had enteric fever in August, 1907. In August and September, 1908, an outbreak of typhoid fever occurred in two adjoining cottar houses, one of which was occupied by the carrier. The persons attacked were the carrier's husband, and a child and a brother-in-law of her neighbour, who worked in a neighbouring town but spent the week-ends at the farm. The two houses were served by one privy which was in a very foul condition.

The bacteriological work in connection with these cases of Dr. Watt was carried out in the Pathological Department of the University of Aberdeen by Dr. A. R. Laing.

Irwin and Houston (1909) of Belfast have put on record a series of typhoid infections due to a female urinary carrier. She had had enteric fever seven years previously when she was a servant in a family at Liscard. Since her illness she had not enjoyed good health and complained of frequent headaches and gastric disturbances. After her recovery from the fever she took another situation in Liscard, but she had not been a month in her new post before the master of the house developed enteric fever. During the next two years she was in different situations but nothing of importance occurred. She then went to Liverpool and while serving in a family there, the son of her mistress developed enteric fever. Finally she went to Belfast, and while she was in service in that city four people living in the same house with her developed typhoid fever. In seven years therefore six people living in the same houses with her had contracted this disease. The urine of this woman contained large numbers of typhoid bacilli but the faeces were negative. Her serum gave an incomplete Widal reaction.

Recently Johnstone (1910–*a*) has reported to the Local Government Board on the association of carriers with endemic typhoid fever in a small Buckinghamshire hamlet. This hamlet (Jennet Hill) consists merely of a few cottages distributed in two groups, (1) a row of 10 dwellings known as Lailey's Row, facing upon a cul-de-sac off the main road between Stanford Dingley and Clay Cross, and (2) nine dwellings scattered irregularly along the same road in the direction of Stanford Dingley and in the direction of Clay Cross. The population of Jennet Hill itself is not more than 80 persons and if the neighbouring hamlets of Stanford Dingley, Clay Hill and Bucklebury Common be added, the population of Jennet Hill and its vicinity probably does not amount to 400.

During the period 1893–1907, 36 cases of enteric fever were notified from the rural district outside the vicinity of Jennet Hill with a population of about 15,000, while from Jennet Hill itself and its vicinity 26 cases were notified. During the period 1896–1907, 25 cases were notified from Jennet Hill and its vicinity while only 24 were notified from the remainder of the rural district. Jennet Hill itself, with a population of 80 people, supplied no fewer than 16 of these 25 cases.

The following table shows the number of cases of enteric fever year by year in the vicinity of Jennet Hill and in the remainder of the rural district of Bradfield respectively, during the period 1893–1907.

	Jennet Hill.	Rest of Rural District.
1893 ...	1	1
1894 ...	–	4
1895 ...	–	7
1896 ...	4	1
1897 ...	8	2
1898 ...	2	3
1899 ...	5	2
1900 ...	1	2
1901 ...	–	6
1902 ...	2	2
1903 ...	–	–
1904 ...	3	–
1905 ...	–	3
1906 ...	1	1
1907 ...	4	2

A marked lack of correspondence between the two parts of the rural district is evident in most years, especially in 1894, 1895, 1897 and 1901, and although the total number of cases was small, the discrepancy suggested the existence of some influence which affected more particularly the neighbourhood of Jennet Hill.

In 1908 an enquiry was made by Dr. Johnstone with a view to ascertaining the cause of this special incidence of enteric fever on Jennet Hill, and in this connexion attention was at first mainly directed to water supply, milk supply, uncooked foods, mineral waters, and excrement-disposal. The evidence on these points must be consulted in the original, but it is sufficient to note here that no satisfactory solution of the excessive incidence of enteric fever on Jennet Hill was reached as the result of this enquiry.

The question then arose as to the possibility of carriers playing a part in the dissemination of enteric. Particular attention was directed to Lailey's Row, as only four of the ten houses composing this row had escaped the fever. Moreover, three of these four houses had but few inhabitants, and these of an age which would render them little susceptible to the disease. Circumstances connected with the occurrence of further cases of enteric fever in 1909, at Lailey's Row, and also in relation with a family that had until recently resided there, strengthened the suspicion that a carrier might be the disseminating agency of the disease. On March 27th, 1909, a boy of six, living a No. 8, Lailey's Row, developed enteric fever. This boy came to Jennet Hill in October, 1908, with his family, consisting of father, mother, and another brother aged 14. He had not been in contact with any known case of enteric fever and he had partaken of no suspicious food or drink.

The former occupants of No. 8, Lailey's Row had gone to a house about three miles away, and two persons were notified as suffering from enteric fever shortly after their return (March 1909) from a visit to this house.

In May a child of one year, residing at No. 9, Lailey's Row, took ill. She had been in this house since October 18th, 1908. The symptoms were obscure but not inconsistent with a diagnosis of typhoid fever, although examination of the stools in the third week after onset was negative.

In the meantime endeavours were being made to obtain samples of excreta (fæces and urine) and samples of blood from the inhabitants of Jennet Hill, and especially from those living in Lailey's Row. Great difficulty was experienced, but ultimately samples of fæces and urine were got from 18 persons, 14 of whom resided in Lailey's Row, also a sample of fæces from another person who formerly lived in No. 8, Lailey's Row. Blood samples were received from 15 persons, all residing in Lailey's Row. None of these persons were known to have had enteric fever. Six, however, gave a positive Widal reaction (1 in 100), while one gave a partial reaction (1 in 50). Four of the samples of fæces contained typhoid bacilli in large numbers, and repeated examinations of these were made :

A. Positive on May 13th, 1909, June 18th, July 3rd. Negative on June 4th and July 16th.
B. Positive on June 4th and July 16th.
C. Positive on June 4th and July 16th.
D. Positive on May 18th, June 2nd, July 9th. Negative on July 24th.

The sera of A, B and D gave a negative Widal reaction, while that of C gave a positive reaction.

The carriers A, B and C belonged to one family, being mother, father and son respectively. The mother presented no history of enteric fever. In 1888 she came to reside at Clay Hill, next door to the house in which a case occurred in 1893. She stated that, while at Clay Hill her husband B. and her two sons, one of whom was C., had enteric fever in April, 1891. In October, 1893, she removed to No. 9, Lailey's Row, but no cases were notified from Jennet Hill till July, 1896. There may have been unrecognised cases, however. From 1896 onwards cases continued to crop up in Lailey's Row and its neighbourhood, seven of them occurring in the houses next door to A.

The husband and son were both difficult persons to deal with, and there was doubt as to whether the samples of fæces received from them were samples of their own fæces or of the mother's fæces.

The carrier D. was a married woman who came to Lailey's Row in September, 1903. She had no history of enteric fever, nor was there any history of enteric fever in families with which she had lived as a domestic servant. In her own family no case of enteric fever is known to have occurred until October, 1906, when her husband was attacked. Two cases (see above) occurred in connexion with the house she has occupied since leaving Lailey's Row.

As only a limited number of examinations was practicable, it appeared possible that there might be other carriers at Jennet Hill; although the detection of two undoubted carriers as well as of two persons in whom the presence of this condition is not yet free from doubt, is sufficiently remarkable in so small a community.

Hilgermann (1908) reports a series of carrier infections in the district of Coblenz (seven carriers). One or two of these (house cases) may be referred to in this chapter.

An old woman of 71 years had long been suspected of causing fresh typhoid infections which broke out from time to time among the newly-imported servants. She had absolutely refused, however, to supply specimens of her fæces for examination. In 1907 another series of three cases occurred in her house. Samples were now insisted upon and obtained and her fæces gave a pure culture of typhoid bacilli. It was ascertained as the result of further enquiry that from 1895 to 1907 (she herself had had enteric fever in 1894) she had infected 15 persons altogether, viz., 1895, one case; 1900, two cases; 1902, two cases; 1903, three cases; 1905, four cases; 1907, three cases.

The other six carriers, all of whom were middle-aged females, had each given rise to one or two infections only, and that too, although, in Hilgermann's view, they must have been in all probability excreting typhoid bacilli continuously. Many instances of intermittent infectivity of carriers are discussed throughout this memoir, but some data may be given here which tend to show that, though infections appear to be particularly frequent among persons coming for the first time into contact with carriers (*vide* Conradi's view, Chapter XII.), there are numerous cases showing that persons who have been a very considerable time in association with a carrier may suddenly contract infection.

Thus one of Hilgermann's carriers (female) after a lapse of five years after her primary attack, infected two persons, with one of whom she had had constant social intercourse. Another carrier (two years after her primary attack) infected her nephew who had been a year with her in the house. Also a case of marital infection occurred on this occasion through the agency of a female carrier. This woman had caused in 1904 a severe outbreak of typhoid fever in the Bavarian Pfalz. Three years later her husband contracted the fever. It appeared that this woman had managed to escape the continual supervision of the typhoid station by frequently changing her abode. She had apparently paid no attention to instructions as to disinfection.

Similar cases of marital infection have not frequently been recorded, and it would appear that in some instances at least the carrier-state may not have been acquired as the result of any obvious precedent infection. Mayer (1908) records such a case:—

On 23rd September, 1902, a servant girl in "D" entered on her service in the place of a sister who was ill with typhoid fever and in hospital. Later, on 5th October, this girl herself contracted typhoid fever. After some years she married a certain Johannes H. in "O." A small epidemic occurred in this hamlet, and there was an investigation, with the result that both Johannes H. and his wife were found to be chronic carriers. The husband, so far as he could remember, had never suffered from any abdominal disturbance, and the only conclusion that could be arrived at was, that he had become a temporary carrier as the result of association with his wife, who after her attack in 1902 continued to excrete typhoid bacilli. From being a temporary carrier he had developed into the chronic stage.

We have to bear in mind not only the possibility of marital cases like the above, but also of the occurrence of multiple carriers in a single family. Fornet (1909) who has recently employed this fact in support of his view that the carrier-state is an immunity-phenomenon, reports that in the course of the typhoid campaign in

South-West Germany, no fewer than 26 families were discovered in which at least two and sometimes three members were carriers.

I shall discuss in Chapter XII. Fornet's view as to the nature of the carrier-state, and the evidence he adduces in support of his view, but I may explain here that his belief is, that the carrier-state is the consequence of a symptomless re-infection, and that the bacilli shed by the chronic carrier may not necessarily be the lineal descendants of the strain which caused the primary infection. The multiple occurrence of carriers in families he would explain on the assumption that all were similarly exposed both to the conditions which rendered the primary infection possible, and to those which resulted in the second or symptomless infection, culminating in the carrier-state.

It would take too much space to refer even in summary terms to the extraordinary chain of typhoid cases which Mayer, G. (1910) has recently put on record in summing up his investigations into endemic typhoid fever in the Bavarian Pfalz during the period 1903–1908. Accompanying his report is a remarkable "Stammbaum" or genealogical tree in which 196 cases appear, all of which he attributes, recently or remotely to contact with one single case. The report must be consulted in the original, but it may be noted that 13 chronic carriers make their appearance in the table, and to these Mayer attributes prime importance in the spread of endemic typhoid fever.

Further interesting house cases and village cases have been reported by Seitz (1909) of Berlin, and Schumacher (1909-*b*) of Trier, the latter of whom has also contributed certain valuable data which will be referred to in the chapter on the statistics of carrier-infectivity (Chapter XIII.).

CHAPTER IV.

INSTANCES OF INFECTIVITY OF CARRIERS—*contd.*

Milk-Borne Cases.

In the foregoing section illustrative cases have been recorded of small outbreaks of enteric fever in individual houses or neighbouring groups of houses, due to association, of diverse kinds, with carriers.

The transmission of infection from the carrier to the healthy, has been in many cases through food-stuffs contaminated by the carrier, but the exact history of the infective agent in its passage to the new host, especially in the absence of cleanly personal habits either on the part of the carrier or his or her associates, cannot in all cases be satisfactorily determined.

In the milk-spread cases which have been recorded during the last few years, the infection has taken hold of comparatively large groups of cases and has been of a more or less explosive character.

In the cases now to be described the fountain head of the infection has proved to be some worker in the dairy from which the attacked consumers obtained their milk supply. I shall first refer to the outbreak recorded by Kossel (1907).

In the summer of 1906, 25 cases of typhoid fever occurred in a town of 60,700 inhabitants. These occurred in groups during the months of May (three cases), June (five cases), July (six cases), and August (11 cases).

Twenty-one out of the 25 cases obtained their milk from the same milk shop in "O." The milk was often drunk raw but in two cases it was boiled, the unboiled cream being used, however, in the preparation of ice pudding. The hygienic arrangements of the milk shop were not satisfactory but in spite of the improvements carried out in view of the earlier cases, a further outburst of cases took place in August. It was therefore suspected that the milk became infected at the farms supplying the milk shop. Three different farms supplied milk, but as one of these also sent milk to a large town "F," where, during November 1905–March 1906, numerous cases of enteric fever had occurred, suspicion naturally attached itself to this particular farm. The excreta of 15 persons at the farm were examined and on 29th October, 1906, a carrier was discovered in the person of a male who fed the swine and who also milked 5–10 cows daily. This person presented no history of typhoid fever. He had been employed for 20 years at the farm but he came originally from a village "B" where typhoid fever had been epidemic. Repeated examinations of the faeces of this man were positive and he was accordingly forbidden to milk. The expectation that no further cases would occur was not realised, for in May, 1907, a single case occurred in "F," also attributable to milk from this farm. On enquiry it was found that the swine-feeder, contrary to orders, was again employed in the dairy.

From the Strassburg Institute two outbreaks are reported by Kayser (1906–*b*). On 23rd, 29th and 30th March, 1905 five people living in different streets of the same quarter of Strassburg fell ill with typhoid fever, and one died. All had drank raw milk procured from a milk-seller "H." This man kept a book in which were noted the names of the farms supplying the milk through him to his various customers and from this book it was found that the milk consumed by the five cases came from two farms in the country district round Strassburg. On enquiry at these houses all were found healthy. One boy of 12, however, was found to have had an indefinite illness about six months before. His stools were examined on 25th April, 1905, and found to contain large numbers of typhoid bacilli. According to Kayser the milk might have become contaminated in various ways. He states that it might have been soiled directly by liquid manure from the cow-shed or the milk-pails may have been washed out with water from an unsatisfactory well situated close to the privy. All the other members of the household, including the mother, who suffered from gall stones, had negative fæces.

In the other farm the hygienic precautions taken in connexion with the milk-operations were certainly bad, but no evidence of infection could be found.

In the same year another small milk-borne epidemic occurred in Strassburg, involving 17 cases, with two deaths. The cases arose in two groups, *viz.*, eight between 5th and 23rd June, 1905, and nine between the commencement and the 26th of August. All had drunk raw milk coming from the same milk shop which sold mixed milk only. It was therefore, with some difficulty, and much touring among the farmers who supplied the milk that the enquiry could be prosecuted. In the course of the investigation, information was received that in a certain family D. a typhoid case had occurred in the past. Serum tests were made from the members of this family and that of Frau D. gave a positive reaction on 25th August. On 27th September the fæces of the members of this family were examined, and in those of Frau D. who was engaged in the milk business the typhoid bacillus was demonstrated. The milk from this particular house was ordered to be pasteurised daily before being offered for sale. No further cases occurred which could be brought into relationship with the dairy.

Chambers and Buchanan (1908), report an outbreak of milk-borne enteric in Glasgow associated with a carrier case. The notifications suggested two distinct waves of infection. The first was irregular and involved eight cases. After a lapse of six days during which no notifications were received, the second wave arose which was maintained unbroken till the end of the epidemic. In the authors' view this second wave presented the true characters of a milk-borne epidemic, viz., rapid increase of the daily notifications and of the numbers sickening simultaneously.

The irregular character of the first wave was explained by the discovery of a chronic carrier ; the secondary wave arose because one of the cases infected by the carrier was a member of a family supplying a portion of the milk. The carrier was a milk woman, who had a history of previous association with enteric fever. Sixteen years previously she had had enteric fever along with most of her family.

Lumsden and Woodward (1909) record a milk outbreak in Washington involving 54 cases. Of these, 33 received milk from a milk dealer A. and 21 from a milk dealer B. During the twelve months preceding this outbreak no cases had occurred in households supplied by A. while 7 cases had occurred in households supplied by B. At the beginning of this outbreak the prevalence of typhoid fever generally in the district of Columbia was on the decline. Only the sections of the city, supplied with milk by these two dealers, were involved, and in these sections the cases were confined to persons consuming milk from these two dealers. Among the customers of other dairymen supplying the same section of Washington, there was no unusual number of cases.

Forty-five households were affected and in eight instances two or more members of the same household took ill. There were 15 instances in which those members of the household who used milk freely were affected, while those who used none or used it sparingly, escaped. There were eight fatal cases, *i.e.*, a mortality rate of 14·8 per cent.

The following table shows the distribution of the cases according to age and sex.

Age-Groups.	Number of Cases.		
	Male.	Female.	Total.
0–4	4	1	5
5–9	5	8	13
10–14	5	3	8
15–19	2	2	4
20–24	3	3	6
25–29	1	6	7
30–34	3	1	4
35–39	1	2	3
40–44	0	1	1
45–49	0	0	0
50–54	0	0	0
55–59	0	0	0
60–64	1	1	2
65–69	0	1	1
Totals ...	25	29	54

Thus the majority of the cases were among children, about 50 per cent. of the cases being in persons under 15 years of age.

The following particulars with regard to the source of the milk delivered by the two dealers A. and B. are taken from an account of this outbreak in a Bulletin of the Hygiene Laboratory by Rosenau, Lumsden and Kastle (1909).

The dealer A. received milk from his own dairy farm and also a daily supply of 40 gallons from the dairy farm of a Mrs. X. Among the consumers of this mixed milk 33 cases of typhoid fever occurred with onsets of illness dating from 24th September to 22nd October.

The dealer B. received milk from 21 farms including a daily supply of 20 gallons from the farm of the same Mrs. X. Among his clients, 21 cases of typhoid fever occurred with onsets of illness dating from 24th September to 24th October.

Mrs. X. in addition to supplying the dealers A. and B. retailed 4 gallons daily to 11 households in one of which three cases of fever occurred with onsets of illness dating from 3rd October to 17th October.

The farm of Mrs. X. was therefore suspected as the source of the infection and as there had been no suspicious illnesses on this farm or in its neighbourhood, the possibility of a carrier suggested itself. Specimens of stools and urine from all the 13 persons on the farm were examined and all were negative except the fæces of Mrs. X. This woman had had typhoid fever 18 years before and had been in excellent health since. She had more to do with handling the milk than any of the others concerned. The milk was liable to be contaminated in other ways, as Mrs. X's. excreta were being deposited in an open privy on the place.

From 16th October, 1908, when Mrs. X. was discovered to be a carrier, the sale of milk from this farm was discontinued by order of the health officer. Eight days later (24th October) the last cases occurring among the customers of A. and B. had their definite onset of typhoid fever.

Judging by the dates of onset in the different cases, the infection appeared to have been more or less constantly in the milk for about one month. Mrs. X. had been in the dairy business for five years and it is remarkable that infection had not sooner occurred. No further specimens of her excreta could be obtained.

One of the most instructive milk-spread epidemics due to carrier infection is that reported by Scheller (1908).

For fourteen years (1894–1907) enteric fever had been prevalent on an estate in the neighbourhood of Königsberg. Thirty-two persons had been certainly infected, but there may have been many more, who had slight attacks only. The people affected had all to do with the estate and there were no cases notified in the village adjoining the estate. The evidence did not point to the water supply as the source of infection, and measures of house disinfection were fruitless in stemming the outbreaks. An extensive investigation was then undertaken from the carrier point of view.

Eight of the 32 persons attacked had their own cow, while 23 others received their milk regularly from the estate. In one case it was no longer possible to ascertain whether the family concerned had possessed a cow of their own or not. The total number of people who were supplied with milk from the estate was about 40, while the number who possessed their own cow was 140. With regard to the 8 cases of this latter series, it was ascertained that though they had their own cows, they applied for milk to the estate when the cows went " dry." The presumption was therefore strong that some relationship would be found between the milk supply from the estate and the cases of enteric fever. The milk that was not consumed on the spot was not sold, but was employed for the feeding of swine. Only the butter was sold to certain people and amongst these no cases of typhoid fever occurred. It was thus explained why the epidemic remained a local one.

The personnel of the dairy was then enquired into. One woman, Frau U., was found to have had typhoid fever 17 years previously. She had been engaged on the estate for about thirty years. From the estate books it was ascertained that she had commenced dairy-work 14 years before, and just a short time before the occurrence of the first case of typhoid fever. Her stools contained typhoid bacilli practically in pure culture, and they were occasionally demonstrable in the urine.

Bacteriological investigation was then made of the excreta of the 40 persons who consumed the milk from the estate, or who assisted in any capacity in the dairy work. Of these 40 persons no fewer than 18 were found to be carriers. One was the woman above mentioned. Of the others, four had had enteric some considerable time previously, while in the remaining 13 no record of a previous attack could be ascertained. The four carriers who had had enteric fever previously could have played no part in spreading the infection by milk, as they had never had anything to do with its preparation.

A large proportion of the 140 persons who received no milk from the estate was also examined but with negative results.

The point to be determined now was whether the woman already mentioned was a genuine chronic carrier or whether the other 17 carriers were also to be classed as such.

It may be noted here that these 17 persons were examined on three occasions at intervals of 12 days. Four were found to be passing typhoid bacilli both in the stools and in the urine, seven in the stools only and six in the urine only. The following test was made. Frau U. was discharged from her dairy-work and all the other carriers who were engaged in the milk business were strictly enjoined to wash their hands in lysol before milking. Further, the milk that was not used for butter was boiled before distribution. The urinary carriers also received urotropin. After a month under this regime all the carriers were again examined when it was found that Frau U. was still discharging bacilli in large numbers while repeated examination of the others (at 15 day intervals) gave negative results. From this it was inferred that Frau U. was a genuine chronic carrier while the other 17 were only temporary carriers.

Scheller believed on grounds which in the light of more recent knowledge, appear insufficient, that he had discovered a type of carrier in which the typhoid bacilli lead a true saprophytic existence in the intestinal canal and cause no disturbance whatever in the organism of the host.

Lentz had previously held the views (1) that a large proportion of these transitory carriers had really reacted to the presence of the typhoid bacilli by slight and possibly unnoticed symptoms, and (2) that those who did not have symptoms even of the slightest order, were still to be classed as "symptomless" typhoid cases in view of the fact that the agglutinin reaction in such cases rose to the same titre as in clinically typical enteric cases. With this latter statement of Lentz, Scheller does not agree as he had noted the absence of agglutinin reaction in some of these cases, while in others he had undoubtedly observed as high a titre as 1 in 2,000. The 17 temporary carriers who ceased to carry, as already described, Scheller preferred to classify in a new group of "Typhusbazillenzwischenträger" (intermediate carriers).

The view is open to criticism for the following reasons :—In the first place, 4 of these 17 carriers had had a definite primary infection, and the actual number of examinations was only three during a period of one month. Without further evidence, therefore, these four persons would not properly be classed as temporary carriers.

In the second place, with regard to the remaining 13 who had never had the slightest symptoms of typhoid fever, one would wish to know whether any of them developed the disease at a later period, as the possibility of a prolonged incubation stage is now well recognised. It is not disputed that this purely saprophytic growth may in some cases take place, but much fuller evidence is demanded before we can admit that such cases have never at any time exhibited symptoms either clinical or serological.

I shall now refer to an extensive series of outbreaks in Aberdeenshire associated with a female carrier who during a large number of years had managed dairy farms.

Watt, Medical Officer of Health, Aberdeenshire (1909), in his annual report on the health of the County of Aberdeen for the year 1908, records that 10 of the 38 cases of typhoid fever notified were traceable to carrier cases. I am indebted to Dr. Watt for furnishing me with particulars regarding the outbreaks associated with these carriers, one of whom is eclipsed only by the Folkestone carrier (*see* pp. 51–56), in so far as the number of her victims is concerned. This carrier, Miss S., a woman of 54 years, was found in connection with an outbreak of enteric fever on a dairy-farm "T" in Aberdeenshire during the summer of 1908. Three servants were attacked (two males and a female) two of whom died. Miss S., who with her brother occupied this farm, had had enteric fever in 1877 when she was 22 years of age. Enquiry showed that since that date a long series of typhoid cases had cropped up at the various dairy farms which she and her brother had managed during these 31 years, and also in Aberdeen, where milk-borne outbreaks traceable to these farms periodically occurred. The following data ascertained by Dr. Watt probably do not exhaust all the cases for which this woman was responsible :—

Farm I.	"G."	Autumn, 1877. Three cases. Brother of Miss S. Female servant, male servant.
		July, 1878. Two cases. Male servant, female servant.
		Spring, 1882. One case. Male servant.
		Summer, 1883. Two cases. Male servant, female servant.
		Summer, 1885. Two cases. Both male servants.
		August, 1897. Two cases. Male servants.
		November, 1898. Two cases. Female servant, male servant (died).
Farm II.	"N."	No cases.
Farm III.	"M."	August, 1900. One case. Male servant (died).
		January–March, 1901, Two cases. Male servants.
		September, 1902. One case. Male servant.
		September, 1903. One case. Maid servant.
		January, 1904. Two cases. Male servant, female servant.
		September, 1905. One case. Male servant.
Farm IV.	"T."	Summer, 1908. Three cases. Two male servants, one female servant (died).

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Besides these cases on the farms, an outbreak in Aberdeen (November, 1898–January, 1899) involving 26 cases, was found to be connected with a dairy supplied by milk from farm "G." (*See* Report by Prof. Matthew Hay for the City of Aberdeen, November, 1899.)

From June, 1900–31st March, 1902, the milk from farm "M" had been sent to a certain dairy in Aberdeen and the following cases of typhoid fever were ascertained to have occurred among the customers of this dairy during the period 1898–1908.

1898. Four cases. August 1; September 1; December 2.
1899. Four cases. January 1; March 1; June 2.
1900. Seven cases. July 1; September 2; October 2; November 2.
1901. Eight cases. January 2; February 2; March 3; April 1; October 1.
1902. Nil.
1903. Nil.
1904. Four cases. February, April, August, November.
1905. Two cases. May, September.
1906. 1907. 1908. No cases.

Outbreaks in Aberdeen prior to 1898 would also appear to have been associated with farm "G," but the actual facts could not be ascertained. In any case it was certainly suggestive that this farm had been visited in September, 1878, 1882 and also in 1885, by the City medical officers of health in connexion with milk spread-outbreaks in Aberdeen. Probably, were all the facts known, it would be found that the number of cases directly or indirectly attributable to infection from Miss S. during the period 1877–1908 would not fall short of 100.

This carrier suffered from gall stones, for which operation was undertaken with a view to obtaining relief from colic troubles and possibly also with a view to ridding herself of typhoid bacilli. An account of the operation will be found in Chapter IX.

Richards, Medical Officer of Health, Croydon (1910), reports an outbreak of enteric fever in a large country house, associated with a carrier in the person of a milker. The cases arose in the following order:—

Case 1.—1903. The butler of a former tenant. Particulars not now ascertainable.

The present tenant took possession in 1906, and all went well till October, 1908.

Case 2.—Male, aged 26. October 22nd, 1908. Severe attack.

Case 3.—Female who lunched at the house on October 17th, 1908, and on November 4th, fell sick.

Case 4.—Kitchen maid. November 1st, 1908. Left the district after convalescence.

Case 5.—Boy. January 17th, 1910. He lived in one of the adjacent cottages.

Case 6.—Kitchen maid. March 11th, 1910.

On the occurrence of Cases 2, 3, and 4, the premises were thoroughly inspected, and certain defects in the drains made good. Water supply, consumption of shell-fish, and other possible sources of infection were exonerated, after careful enquiry. The excreta of Case 2 were examined with negative results, though his serum reaction was still positive. On the assumption that all the cases except the first had a common origin, suspicion could be attached only to those members of the household who were on the premises in 1908 and 1910. These were three in number, viz., the cook, who entered on her duties about March, 1908 ; a housemaid, who had lived in the house since May, 1904 ; and the milker, whose history will be detailed below.

Neither the cook nor the housemaid presented a history of a typhoid infection or association with enteric cases in other households. The excreta of both were examined with negative results.

The fæces of the milker, however, contained typhoid bacilli. This man never had enteric fever, but his wife had an attack in 1894, when they were living in another village. He came to this country house in 1902, and was milking at the time when Case 1 was infected in 1903. He left the district in September, 1906, but returned in October, 1908, when he entered on his present duties. Case 2 fell ill about October 22nd. It is important to note that between September, 1906, and October, 1908, this man was employed in a dairy in another district where a large amount of milk and butter was sold, but during that time there do not appear to have been any cases of enteric fever among the customers.

The following facts were ascertained with regard to the consumption of milk by the persons attacked :—

Case 1.—Cannot be traced, but as he was an indoor servant he doubtless consumed the milk supplied to the house.

Case 2.—Not only took milk, but was especially fond of cream.

Case 3.—Believed to have had cream in coffee and probably with fruit or tart.

Case 4.—Consumed both cream and milk.

Case 5.—Came to the house daily for milk.

Case 6.—Consumed milk and cream.

The milk was consumed mostly in the house, some being set for cream and some made into butter. The excess milk was disposed of in variable quantities to eight adjacent cottages, including the one occupied by Case 5.

That only six persons were attacked, although about 47 persons consumed the milk at various times, is largely accounted for by the fact that the quantity of milk consumed per head was small except in the large house, where most of the cases occurred. Further, as the history of other milk-spread epidemics due to carriers has shown, the opportunities of successful infection are notoriously intermittent. Dr. Richards suggests that the absence of infections during the milker's sojourn in a large dairy during 1906–1908 may have been due to the necessarily greater dilution of the poison which would thus act as a safeguard. The stools of this milker have since been examined by me on 19th May, 1910, with positive results. Those of his wife and daughter were, however, negative.

Recently a report by R. W. Johnstone (1910–*b*), on the recurrent prevalence of enteric fever in the Folkestone Urban District, has been submitted to the Local Government Board. The report is a most exhaustive one, and the details will be read with the greatest interest by all epidemiologists. Here I must confine myself to a brief survey of the enquiry.

The Urban District of Folkestone had at the Census of 1901 a population of 30,379, and in the middle of 1908 it was estimated to be 35,580. In the year 1901, Dr. Theodore Thomson had reported to the Local Government Board on recurrent enteric fever in that district, and had made careful enquiry into water supply, refuse and excrement disposal, sewerage and drainage, and the conditions prevailing in the various cowsheds, dairies and milkshops. He found that no satisfactory explanation of the repeated occurrences of enteric fever in Folkestone could be obtained by a consideration of the water supply and other sanitary conditions. He was able, however, to show that in certain years, viz., 1896, 1897, 1899 and 1900, milk was a prominent factor in the dissemination of enteric fever in Folkestone, while it may have been responsible for a small share of the fever in 1898. He also noticed that a certain milker had worked upon the three different milk farms which were associated with the dissemination of enteric fever in the years 1896, 1897 and 1899. At that time, however (1901), there was no knowledge of the typhoid-carrier, and Dr. Thomson had dismissed the coincidence with the remark "no milkman, even if uncleanly in his ways, can convey infective material unless the material be there to convey." Dr. Johnstone, who took up the enquiry in August, 1909, found that the facts elicited by Dr. Thomson with regard to water supply and general sanitary conditions still held good, and proceeded to enquire into the milk question.

Before detailing his results, I append the following tables (extracted from Dr. Johnstone's report) relative to the incidence of enteric fever in Folkestone from 1893 to 1909.

Table showing the number of deaths from enteric fever and the number of cases notified in the Urban District of Folkestone during the period 1893–1909. For comparison, similar figures are given for the neighbouring Urban Districts of Hythe (pop. 1901, 5,551), Sandgate (pop. 1901, 2,294), and Cheriton (pop. 1901, 7,091), and for the Rural District of Elham (pop. 1901, 6,813).

—	Folkestone Urban District.		Hythe Urban District.		Sandgate Urban District.		Elham Rural District.		Cheriton Urban District.	
	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.
1893	—	5	—	4	—	—	1	1		
1894	2	7	—	1	—	3	1	3		
1895	—	10	1	2	1	3	3	4		
1896	4	18	1	1	1	1	1	5		
1897	4	40	—	3	—	1	1	1		
1898	8	36	1	3	—	—	—	2		
1899	16	87	—	—	—	1	—	2	—	—
1900	5	50	—	—	1	9	—	1	—	—
1901	3	14	1	2	—	2	—	1	—	1
1902	6	26	—	2	—	2	1	2	1	3
1903	2	16	—	1	—	—	1	1	1	—
1904	1	7	—	3	—	2	—	2	—	—
1905	—	6	—	—	—	—	—	—	—	—
1906	—	11	—	2	—	—	—	1	1	1
1907	1	20	—	—	—	—	—	1	—	—
1908	—	9	—	—	—	—	1	3	—	—
1909	1	19	—	1	—	—	1	2	—	—
Total	53	381	4	25	3	24	11	32	3	5

From the figures it will be seen that enteric fever began to increase in Folkestone Urban District in 1896 and that it attained its maximum prevalence in 1899, subsiding in 1901 to show minor recrudescence in 1902, 1903, 1907 and 1909. No correspondence can be traced between the degree of prevalence of the fever in the other districts and that in Folkestone.

Table showing the incidence of enteric fever as regards the age and sex of persons attacked during the period 1896–1909.

Year.	-5	-15	-25	-35	-45	+45	Total at all ages.	Males	Females.	Over Age 15.	
										Males.	Females.
1896 ...	2	8	4	3	1	—	18	3	15	2	6
1897 ...	2	13	15	8	—	2	40	13	27	6	19
1898 ...	3	10	9	10	2	2	36	18	18	11	12
1899 ...	2	22	28	18	12	5	87	38	49	25	38
1900 ...	—	15	24	6	5	—	50	16	34	10	25
1901 ...	1	3	5	3	1	1	14	5	9	3	7
1902 ...	1	3	10	7	2	2	25	12	13	10	11
1903 ...	1	7	3	2	2	1	16	8	8	3	5
1904 ...	—	2	2	2	1	—	7	4	3	3	2
1905 ...	—	1	2	1	1	1	6	3	3	2	3
1906 ...	—	1	2	6	—	2	11	9	2	8	2
1907 ...	2	5	5	4	—	4	20	6	14	3	10
1908 ...	—	3	4	2	—	—	9	5	4	3	3
1909 ...	1	11	—	2	2	2	18	9	9	4	2
Whole period.	15	104	113	74	29	22	357	149	208	93	145

N.B.—In considering these figures it has to be borne in mind that at the Census of 1891, females to males in Folkestone were as 138 to 100, whereas in England and Wales the proportion was 108 to 100. At the Census of 1901 females to males in Folkestone were as 136 to 100 and in England and Wales as 107 to 100.

Results of Dr. Johnstone's enquiry :

During the period 1901–1909 the local Inspector of Nuisances had made careful inquiries which seemed to indicate that the milker referred to by Dr. Thomson in his report of 1901 was connected in other years with milk farms said to be associated with the dissemination of enteric fever. Samples of this man's excreta were now procured (fæces and urine) and submitted to bacteriological examination. The typhoid bacillus was isolated from the fæces on the five occasions on which samples were taken, viz., 31st August, 1909, 6th September, 1909, 11th September, 1909, 25th September, 1909, and 19th October, 1909. The urine was always negative. This milker N. was, therefore, a typhoid carrier. He was a man of about 60 years of age, enjoying excellent health. To his knowledge he had never suffered from enteric fever nor had his wife or any of his children while living with him. The only severe illness he was able to recall occurred about 30 years ago. At that time he had suffered from lassitude, lack of appetite, and general malaise, and though he was not bad enough to take to his bed, the illness had left a lively impression on him and his wife. Up to the age of 26, N. had been a sailor. He then took up farm work, but did not become a regular milker till April, 1893, when he came to a farm in the Elham Rural District, close to Folkestone.

From that time till August, 1909, he was constantly employed as cowman and milker on various farms near Folkestone, viz. :—

No. 1 Farm, April, 1893–October 11th, 1895, in Elham Rural District.

No. 2 Farm, October 11th, 1895-October 11th, 1896, in Elham Rural District.

No. 3 Farm, October 11th, 1896–October 11th, 1898, in Dover Rural District.

No. 4 Farm, October 11th, 1898–October 11th, 1902, in Elham Rural District.

No. 5 Farm, October 11th, 1902–October 11th, 1909, in Elham Rural District.

During N.'s stay at No. 1 farm there were five cases of enteric fever at the farm, viz., son and daughter of the farmer, a visitor, a maid-servant, and a charwoman.

At No. 2 farm there was one case of enteric fever while N. worked there.

At No. 4 farm two of the farmer's daughters had enteric fever while N. worked there.

Table showing year by year the number of cases of enteric fever notified in the Urban Districts of Folkestone, Hythe, Sandgate, and the Rural District of Elham during the period 1893–1909.

In separate columns are shown the number of persons who contracted the fever outside the district (imported cases) and the number of persons who lived in houses deriving their milk supply wholly or in part from a farm on which N. worked as a milker at the time of infection (N. cases).

—	Folkestone Urban District.			Hythe Urban District.			Sandgate Urban District.			Elham Rural District.		
	Total Cases.	Imported Cases.	N. Cases.	Total Cases.	Imported Cases.	N. Cases.	Total Cases.	Imported Cases.	N. Cases.	Total Cases.	Imported Cases.	N. Cases.
1893	5	—	—	4	—	—	—	—	—	1	—	1
1894	7	—	—	1	—	—	3	—	—	3	—	3
1895	10	—	—	2	—	—	3	—	3	4	2	1
1896	18	1	13	1	—	1	1	—	—	5	—	3
1897	49	3	20	3	1	—	1	—	—	1	—	1
1898	36	1	14	3	2	—	—	—	—	2	1	—
1899	87	2	66	—	—	—	1	—	—	2	—	2
1900	50	5	38	—	—	—	9	—	—	1	—	—
1901	14	3	10	2	—	2	2	—	—	1	—	—
1902	26	4	15	2	1	1	2	—	—	2	—	—
1903	16	5	7	1	—	—	—	—	—	1	—	—
1904	7	—	4	3	2	—	2	—	—	2	—	1
1905	6	1	—	—	—	—	—	—	—	—	—	—
1906	11	2	1	2	—	—	—	—	—	1	—	1
1907	20	6	3	—	—	—	—	—	—	1	1	—
1908	9	2	3	—	—	—	—	—	—	3	—	2
1909	19	1	13	1	—	—	—	—	—	1	—	1
Totals ...	381	36	207	25	6	4	24	—	3	31	4	16

For particulars with regard to the milk supply in the various years and the enteric outbreaks associated with it, the original report must be consulted.

In the 14-year period 1896–1909, 359 cases of enteric fever are known to have occurred in Folkestone Urban District, and of these 36 are known to have been imported cases. Of the remaining 323 cases, 207 or 64 per cent. are known to have had milk, within three or four weeks preceding their illness, from one or other of the farms on which N. was at the time acting as milker.

Interesting data were obtained relative to the incidence of enteric fever as regards the age and sex of the persons who had taken N.'s milk, and in the following table the figures are set forth :—

—	—5	—15	—25	—35	—45	+45	Total.	Males.	Females.	Over 15.	
										Males.	Females.
1896	1	6	4	2	—	—	13	3	10	1	5
1897	—	8	7	5	—	—	20	7	13	3	9
1898	—	7	4	3	—	—	14	6	8	2	5
1899	3	17	18	13	10	5	66	20	46	16	30
1900	—	14	16	6	2	—	38	11	27	5	19
1901	1	3	3	2	—	1	10	3	7	1	5
1902	1	2	5	2	4	1	15	9	6	7	5
1903	—	3	1	1	1	1	7	3	4	1	3
1904	—	—	2	2	—	—	4	2	2	2	2
1905	—	—	—	—	—	—	—	—	—	—	—
1906	—	—	1	—	—	—	1	1	—	1	—
1907	—	1	2	—	—	—	3	—	3	—	2
1908	—	2	—	1	—	—	3	2	1	1	—
1909	1	8	—	1	1	1	12	4	8	2	1
Total	7	71	63	38	18	9	206	71	135	42	86

A comparison of these figures with those relative to the cases which had not taken N's milk revealed fairly clearly that there was a disproportionate incidence of enteric fever on females and children in the group which had partaken of N's milk. This undue proportional incidence is in itself suggestive of milk-borne infection.

To sum up. N., a typhoid-carrier, worked at five different milk-farms as cowman and milker during the period 1893–1909. Enteric fever broke out at three of these farms during his stay there, and cases of enteric fever also occurred in the neighbourhood of all five of them. On the milk round of each of the five farms there was undue prevalence of the fever at intervals during the time N. worked there, and no such prevalence was observed either before his advent or after his departure. During the period 1896–1909 64 per cent. of the cases of enteric fever infected in Folkestone had been supplied with milk from a farm on which N. was working. Certainly milk from N's farm was supplied in two other districts for three months in 1901 without any known increase of enteric fever in these districts, and no cases of the fever could be attributed to N's milk during the year 1905, but as Johnstone remarks, N. may have been only intermittently infective, and even had his condition been one of continuous infection, it was not inevitable that the infection should always reach the milk-supply. "On the whole facts it may be concluded that for the past 14 years enteric fever has been spread in Folkestone Urban District mainly by milk, and that the milk was infected by N., a typhoid-carrier."

CHAPTER V.

INSTANCES OF INFECTIVITY OF CARRIERS—(*continued*).

Institutional Cases.

A large proportion of typhoid carriers have been found in institutions like asylums, workhouses, private schools, &c., where typhoid fever has been of endemic occurrence. In such establishments the intimate contact prevailing among the inmates must play a large part in facilitating the spread of infection from case to case. In lunatic asylums especially, the filthy personal habits of many insane people are naturally accentuating factors where a carrier or carriers are already in existence. Some attempts have been made to explain the presence of large numbers of carriers in lunatic asylums, and the hypothesis has been put forward that a psychosis is a predisposing factor to the carrying status.

There is no evidence in support of this view, but there is much to be said for the view held by some observers that the proportion of carriers discovered in institutions may ultimately prove not to be unduly large, since the facilities for thoroughly carrying out bacteriological investigations on a large scale are greater than is usually the case elsewhere, and correspondingly increase the probability of detecting the presence of carriers.

Several striking instances of endemic typhoid fever in asylums have been recorded in recent years.

Nieter and Liefmann (1906) of Halle, record observations made in a lunatic asylum at "M," containing 900 female patients, in which, for a number of years, there had been repeated outbreaks of typhoid fever. These outbreaks had always occurred in small groups. Most of the cases were confined to one building containing about 250 inmates. After an examination of the convalescent cases had yielded no carriers, they proceeded to examine all the inmates in this block. In one case of acute dysentery the B. typhosus was found in the fæces along with B. dysenteriae (Flexner). The association was explained by the fact that cases of dysentery and of typhoid fever were isolated in the same block, and it seemed likely that the dysentery patient had got secondarily infected with the typhoid bacillus. Her serum agglutinated B. typhosus in 1 in 100, and B. dysenteriae (Flexner) in 1 in 800.

In another dysentery case they found the typhoid bacillus in the stools but not the dysentery bacillus, and at her death numerous old typhoid cicatrices were found in the small intestine, while the lower bowel showed chronic catarrh. The gall bladder was full of large and small stones, and the typhoid bacillus was present in pure culture in the bile.

Other five carriers were discovered, making seven in all out of a total of 250 inmates. This makes a percentage of 2·8 per cent., which is much higher than that obtained by searching the neighbourhood of typhoid patients (viz., 0·5—0·8 per cent.). All the carriers were women. After isolation of all the carriers it was hoped that no further cases would occur, but this hope was not realised.

In a further report by Nieter (1907) on this asylum, it is stated that four more carriers were discovered during the late summer of 1906, thus making a total of 11. About the latter part of December and the beginning of January, 1907, three new cases of typhoid fever occurred among nurses employed in this same block of 250 inmates, where the seven carriers had been discovered. Another investigation was made and another female carrier was found. This person had never had clinical symptoms of typhoid fever. Paratyphoid bacilli were also present in her fæces.

After an interval of 4–5 months, three fresh cases occurred in another building in which two carriers had been previously found. In this room was a patient who two years before had had typhoid fever. During the first investigation this woman's excreta had been negative, though she had given a positive Widal reaction.

A second examination was now made and this woman was found to be passing typhoid bacilli in her stools. Thirteen carriers had been discovered in this asylum up to 1907.

Nieter mentions that in other asylums several carrier cases had been isolated, viz., Hordt (13 female carriers), Klingemünster (two carriers), Saargemund (two carriers), Merzig (one carrier).

Friedel (1906) reported a striking instance of institutional typhoid fever due to carrier infection, in which foodstuffs, in all probability, formed the intermediate link between the carrier and the new hosts. The institution affected was the Provinzial-Heil-und Pflegeanstalt at Andernach in the Coblenz district. On 1st September, 1905, this asylum contained 650 persons distributed thus :—

Group	A.	Patients, male and female ...	500
„	B.	Nurses, 36 male and 36 female ...	72
„	C.	Staff, various	20
„	D.	Families in detached villas ...	45 persons.

All these groups had the same water supply. Groups A, B and C obtained food from the main kitchen, while the families in group D had their own kitchens.

Before 1901 only occasional cases of typhoid fever considered to have been due to outside infection had occurred. In 1901 two outbreaks arose in different blocks, viz., in May, nine cases (one physician, five male nurses, three male and one female patients), and in October, 12 cases (nine female nurses, one male nurse, one male and one female patient). In May, 1905, seven cases (one male nurse, six male patients), occurred in one male block.

Between 1901 and 1905 there were seven isolated cases, of which six were believed to have contracted the infection inside the building.

In these outbreaks the water supply could not be called in question. The possibility of already infected food coming from outside the institute was ruled out. Suspicion accordingly fell on the kitchen. The food was prepared here and then distributed to the various blocks.

Accordingly all those persons engaged in the dairy or kitchen who were ascertained to have had typhoid fever were examined, but with negative results.

In September, 1905, another outbreak occurred with 35 cases, 8 male nurses, 8 female nurses, 4 males on the staff, 5 male and 10 female patients, but none belonging to Group D.

The fæces and urine of all engaged in the kitchen, wash-house, scullery, dairy and laundry were now examined, whether they had had typhoid fever previously or not, and one female imbecile (65 years), who had been six years in the kitchen was found to be a carrier. She had never had typhoid fever, at least in the institution.

Her serum gave a negative Widal reaction. The chief duty of this woman was the cutting up of potatoes for potato salad and pieces of meat for Fleischsalat and various other salads. There is undoubtedly great danger attached to the consumption of such raw food material which has been contaminated during its preparation, or of cooked material which becomes contaminated before its final consumption in the cold state. In both cases cold storage is indicated as tending to lessen the likelihood of rapid multiplication of the B. typhosus and, therefore, of risk of infection to the consumer.

Ledingham, A. & J. C. G. (1908) have recorded the results of an investigation into the cause of recurring enteric fever in a lunatic asylum in Scotland. This asylum in 1908 contained 92 male and 53 female patients, 8 male and 6 female attendants and 4 female servants. Since 1893 there had been a succession of small outbreaks of typhoid fever in this asylum, the female inmates being principally affected. Also similar outbreaks had occurred periodically in a smaller detached building containing 32 female patients, and situated about five minutes' walk from the main building. Prior to the adoption of the Notification Act in 1891, no authentic records of typhoid fever in this asylum were available. The annexed table shows the incidence of typhoid fever in successive years since 1893, when the first case was notified :

Year.	Total No. of Cases.	Month of Notification.	Main Asylum.	Small Asylum.
1893 ...	2	Mar., July	2	0
1894 ...	0	... ...	0	0
1895 ...	6	July (2), Aug. (3), Dec. (1)	1	5
1896 ...	2	Apr., May	2	0
1897 ...	1	Nov.	0	1
1898 ...	0	... ...	0	0
1899 ...	4	Aug. (1), Nov. (3)	4	0
1900 ...	3	Jan., June, Aug.	1	2
1901 ...	2	Feb., May	2	0
1902 ...	0	... ...	0	0
1903 ...	4	Feb., Mar., Apr , Oct. ...	4	0
1904 ...	3	June, July, Aug.	3	0
1905 ...	0	... ...	0	0
1906 ...	1	April	1	0
1907 ...	3	Feb., Apr., Oct.	2	1
Total ...	31	... ...	22	9

It will be seen that 31 cases in all occurred and 24 of these were females, viz., 21 female patients, three female attendants, six male patients and one male attendant. Nine of the cases proved fatal. The cases arose at no special season of the year, but in individual years the notifications followed each other as a rule very closely. During 1894, 1898, 1902 and 1905 no cases were notified.

The mysterious cropping up of typhoid cases had been a source of great anxiety to the authorities, who had done everything in their power to make the sanitary arrangements of the institution as complete as possible. Repeated analyses of the water supply, both chemically and bacteriologically, threw no light on the etiology of the outbreaks. The sewage was conveyed direct to the sea and the dairy arrangements were in excellent order. The same water supply served several families residing on a farm near the source of the supply, but at no time had cases of enteric fever occurred among them. It was accordingly determined to search for carriers among the inmates. In February, 1907, a start was made by testing the Widal reaction in a group of 43 female patients, and six of these, two of whom had had enteric fever previously (in 1903 and

1904 respectively), gave a well-marked reaction. In the course of this work, however, A. L. contracted a severe attack of typhoid fever, and nothing further was done in the matter till September, 1907, when it was proposed to examine bacteriologically the stools of all the female patients in the asylum. Three female typhoid carriers were thus discovered. The first, G., had been in the asylum (main block) since 1896. She was 35 years of age, and there was no record of a primary infection. Her personal habits were exceedingly filthy. She had not, however, been employed either in the laundry or kitchen. Her serum gave a Widal reaction in a dilution of 1 in 200.

The second carrier, McC., had been in the small detached building since 1895, when she had had an attack of typhoid fever. She was about 60 years of age and was able to walk about and do a little work, but had never been employed in the kitchen. Her habits were cleanly, and occasionally she had assisted in the laundry. Her serum gave a Widal reaction in 1 in 200. It has to be noted that, though there are two separate blocks, much communication goes on between them. The dinners are cooked at the main block and brought over to the smaller block. The clothes are washed also at the main block, but patients from the small block would sometimes assist.

The third female carrier, C., was about 30 years old and had typhoid fever in 1904. She was not of dirty habits, but had never been employed in the kitchen or laundry. Her serum gave a marked Widal reaction.

These three females were isolated as soon as they were discovered to be carriers, and since November, 1907, they have remained in the isolation block with a special attendant.

Since October, 1907, the asylum has enjoyed complete immunity from typhoid fever. There have been 42 females admitted into the asylum during this period and it is proposed to examine all these bacteriologically, and in future to examine each new patient on admission into the asylum.

Eccard (1910) records a very similar experience of endemic typhoid fever in an asylum at Frankenthal in the Pfalz district. This institution contains 650 mental cases in one department, and 250 bodily-sick cases in another. Long before 1901 enteric fever had been of endemic occurrence, but since that year infection had occurred among the women only, the chief focus of the disease being the female block containing 110 " unclean, stupid and noisy " women.

In 1903 this block was gone over with the result that three female carriers were found. These had been housed for a long time in this department and had never been ill. An isolation barrack was put up for them and to this the typhoid cases were also transferred.

In spite of these precautions fresh cases cropped up and the conclusion was come to that some carriers, probably of the intermittent variety, had been missed. This proved to be the case. The investigation was repeated and in June, 1906, another female carrier was found. In December of the same year a fifth carrier, in May, 1907, a sixth, and in July, 1907, a seventh carrier was revealed. The examination of the stools and urine of these last three carriers had given negative results on previous occasions. The stools and urine of the carrier who was discovered in December, 1906, had been examined previously with negative results no fewer than five times, and still it was she who apparently kept the epidemic going, for after her isolation the occurrences of fever ceased, nor have there been any further cases in the three years up to 1909.

The following table shows the incidence of typhoid cases according to months and years from 1901 to 1st August, 1909 :—

Years.	Months.												Totals.
	Jan.	Feb.	Mar.	Apr.	May.	Jun.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	
1901 ...	—	—	—	2	1	1	—	—	—	1	—	—	5
1902 ...	—	—	—	1	1	—	—	—	—	1	—	—	3
1903 ...	—	—	—	—	—	—	—	—	1	4	—	—	5
1904 ...	1	—	1	1	—	—	—	—	1	—	—	—	4
1905 ...	—	—	—	—	—	—	—	—	1	—	—	1	2
1906 ...	—	—	—	—	1	—	—	—	*1	1	—	—	3 – 1
1907 ...	—	—	—	—	—	—	—	—	—	—	—	—	0
1908 ...	—	—	—	—	—	—	—	—	—	—	—	—	0
1909 ...	—	—	—	—	—	—	—	—	—	—	—	—	0

* Imported case.

Reformatory Case.

The female carrier case reported by Davies & Walker Hall (1908) is so well known in this country that I need only refer to the most important features of the outbreaks for which she was responsible. In November, 1906, an outbreak of typhoid fever occurred in an Inebriate Reformatory near Bristol. This institution then contained 240 inmates and 24 resident officers. There had been no visitation of typhoid fever since the opening of the institution in 1899. No cases of typhoid fever existed in the neighbourhood at the time of the outbreak. In September, 1906, a kitchen helper took ill, and in November three more cases occurred in which the suggestion was that the infection was conveyed by milk. One was a female inmate who received an extra allowance of milk daily, as she was nursing ; another was the gardener's wife who lived in a detached cottage and received only milk from the institution. The third was an outdoor policeman who received an allowance of milk for his tea. No explanation of the initial case was forthcoming. Fresh outbreaks occurred in May, 1907, and continued up to

November, viz., May, 1 case; June, nil; July, 6; August, 9; September, 1; October, 2; November, 4, *i.e.*, 23 altogether.

The evidence in the 1907 cases was still stronger against the milk which evidently had some opportunity of being contaminated after sterilization. It was learned that an inmate, Mrs. H. (50 years), employed as cook and dairymaid in the institution had suffered in January, 1901, from typhoid fever. She had been admitted to the Reformatory in April, 1906, and was employed in kitchen work up to October 13th, 1906, when she was entrusted also with the dairy work which she continued up to November, 1907. At Dr. Davies's suggestion she was excluded from kitchen and dairy work on November 13th, and 12 days afterwards, November 25th, the last case of the series occurred. On November 18th, 1907, her serum gave a negative Widal reaction, and the stools and urine were typhoid-free. On November 29th, 1907, the stools also proved negative, but a positive result was obtained on December 20th, 1907. Further examinations on January 20th, February 14th, February 18th, and March 14th were, however, negative. The urine was always negative. The fæces again proved positive on April 14th, 1908. (For further data on the bacteriological examinations of the excreta of this case *see* Chap. XII.) The milk after sterilization was stored in the dairy whence it was measured out for the various blocks by means of a hand-dipper. All the milk passed through her hands. It is evident, therefore, that the milk which was shown to have been the agency by which the fever was disseminated could readily have been infected by Mrs. H.

Enquiry into the past history of this carrier showed that she had been in all probability responsible for enteric outbreaks in at least two other institutions.

In May, 1904, typhoid fever broke out in the Grove House Home for Girls at Brislington, near Bristol. This institution was then occupied by 36 girls (5—15 years) who were boarded out by the Bristol Guardians. From May to the end of September, 26 persons in the institution developed enteric fever. Eight suspicious cases also occurred. Two cases ended fatally.

There had been no typhoid fever in the district for months and the sanitary arrangements of the institution could not be impugned. All attempts to combat the spread of the disease by disinfection, boiling of milk, &c., were fruitless. It appears that Mrs. H. had on February 3rd, 1904, been transferred from the Bristol workhouse to the kitchen at Grove House, Brislington. Her duties were to assist in the kitchen and to cook, and all the milk, which was boiled, passed through her hands. It is notable that she left Grove House Home on September 2nd to take a private situation, and the last case in the institution was notified twenty days later, viz., on September 22nd, 1904.

It was further ascertained that on March 4th, 1905, this carrier became cook at a children's home where there were 30 girls. Nothing happened till May 8th, 1905, when one of the girls developed enteric fever for which no cause could be found. The cook had left at the end of April. No further cases occurred.

I conclude this chapter with certain general observations regarding the occurrence of carriers in asylums and similar institutions. As I have mentioned, the higher frequency of carriers in asylums as compared with that found in the neighbourhood of typhoid cases elsewhere, has been attributed to a psychosis predisposing typhoid-sick lunatics to this condition.

There are, however, certain considerations which tend to discountenance the need for adopting such an explanatory hypothesis as this. In the first place much greater facilities are afforded to one chronic carrier of unclean habits, of infecting her associates, who may then act as temporary carriers or who may become chronic carriers. In the second place, as Eccard suggests, a lunatic typhoid-convalescent of filthy habits is probably always re-infecting herself and so develops into the chronic type. This view has been applied in a wider sense to all chronic carriers by Fornet, who as I have said (*vide* Chapter III.) maintains that the carrier state arises from a symptomless re-infection and is an evidence of immunity in the sense of Wassermann and Citron.

CHAPTER VI.

INSTANCES OF INFECTIVITY OF CARRIERS—(*continued*).

Army Cases.

The association of carriers with occurrences of typhoid fever in army barracks, &c., presents features similar to those met with in civil communities, but it seems advisable for facility of reference to discuss the subject of army carriers in a separate chapter.

The most extensive work which has so far been done in this connection has emanated from the Central Research Institute at Kasauli in India, where an enquiry into the cause and spread of enteric fever was set on foot in 1906 under the guidance of Lieut.-Colonel D. Semple and Captain E. D. W. Greig.

Their first report (Semple and Greig (1908)) on the investigations carried out appeared in 1908 and abundantly confirmed the experiences of the typhoid-stations in South-West Germany. I have referred in a previous chapter (Chapter II.) to certain statistical results collated by them in connexion with the bacteriological examination of convalescents, and it now remains here to record details of the regimental outbreaks of typhoid fever for which carriers were found to be responsible.

The first outbreak occurred in a detachment of the Bedfordshire Regiment at Kasauli. During the month of Angust, 1907, 5 cases of enteric fever occurred in this detachment. Two barracks were involved; each of these was divided into four wards; the cases arose in different rooms and there had been no direct personal communication between the patients. The food supply of the two barracks came from a common cook-house and the latrine and urinal were also in common. As the cases were confined to one detachment the general water and milk supply could be eliminated, Examination was therefore made of the blood, urine and fæces of all the cooks and contacts of this unit with the result that one cook belonging to this detachment was found to be excreting large numbers of typhoid bacilli in his fæces.

The carrier was at once isolated and no further cases occurred.

A definite history of enteric fever in this carrier could not be elicited, but there was a probability that a severe attack of ague (31st December, 1897—10th March, 1898) lasting seventy days may have been an unrecognised typhoid infection. It was also noteworthy that, according to the health registers, from 23rd May to 3rd July, 1899, he had been treated for abscess, which may have been also of typhoidal origin. His Widal reaction was negative, agglutination taking place only in a dilution of 1 in 20.

The second outbreak occurred in the Scottish Rifles (Cameronians). As a result of the examination of a large number of healthy soldiers at Meerut from the different units stationed there, one man belonging to the Scottish Rifles was found to be a carrier. He had never suffered from enteric fever, but had been a nursing orderly on enteric cases. I have already noted (Chapter II.) that these orderlies not infrequently excrete typhoid bacilli without showing any obvious symptoms and are liable to become chronic carriers.

The connexion between this carrier and the particular cases of enteric fever could not be so clearly established as in the first outbreak, but the fact that seven out of the ten cases examined at Meerut came from this particular unit of the Scottish Rifles was considered very significant.

Semple and Greig, in view of the danger that nursing orderlies may contract the disease so slightly as not to report themselves sick, but may nevertheless become carriers, suggest that a special permanent body of trained men should be formed to nurse enteric patients.

An extremely interesting case of carrier infection in an artillery barracks at Wesel has recently been reported by Niepratschk (1909). During the years 1904–1908 this barracks had been, as the author expresses it, a "veritable typhoid-house." Its hygienic conditions were excellent and no source of infection could be traced. Since October, 1902, it had been occupied by the artillery regiment, and on January, 1904, the first case of typhoid fever occurred. During the five years 1904–1908, there had been 31 cases of typhoid fever, of which six ended fatally and four led to invalidity. The cases occurred as follows :—

1904. One case. (January.)
1905. Seven cases. (February, May, October (3), November, December.)
1906. Two cases. (April and October.)
1907. Twenty cases. (Ten between January and June. Ten between September and November.)
1908. One case. (February.)

The first two cases were attributed to infection contracted during Christmas leave, and the third case was also in all probability imported. For the other cases no probable source of infection was forthcoming. Neither in the civil population nor in the other troops of the garrison was the typhoid incidence high. The opinion that water played any part in the spread of the fever had to be abandoned after careful attention paid to the water supply had yielded no result. The hypothesis that a carrier might be at the root of the trouble was then tested, and a commencement was made with an examination of the fæces and urine of the lessee and assistants in the canteen. The cook (a female of 55 years of age) had had enteric fever two years before, and in August, 1907, had suffered from a febrile attack pointing to gall-bladder trouble. Repeated examinations of her fæces and urine were, however, negative, and she gave an absolutely negative Widal reaction. The examinations of the stools and urine of all the other assistants were negative.

Then began a systematic examination of the "Unteroffizieren" of the individual batteries. On 23rd February, 1908, Sergeant B. was found to be excreting large numbers of typhoid bacilli in his urine. No other carriers were found.

The history of this man was as follows :—In the spring of 1901 (5th March to 29th April) he had had a severe attack of enteric fever while serving in a regiment of Dragoons at Tilsit. His urine during the fever had been free from albumin. On 29th April he was sent home to recruit, but eight days later he had a severe relapse and for eight weeks could not be transported. On 20th June he returned to the regimental hospital and remained there till 8th July. At the close of his three years' service in October, 1901, he spent a year at home. On October 1, 1902, he joined the 15th Ulan regiment at Saarburg, where he remained till 1st October, 1903. He then returned home, but enlisted again on 15th June, 1904, in the 1st "Trainbataillon," at Königsberg. With this regiment he remained only one year, and on 15th June, 1905, joined the Artillery regiment at Wesel.

Some suggestive facts were later ascertained with regard to typhoid outbreaks in other regiments to which this man belonged before coming to the Wesel garrison. Thus in the year in which Sergeant B. was in a "Trainbataillon," one case occurred, while during the previous three years there had been no cases in that regiment. Also during his service in an Ulan regiment, 15 cases had occurred in 1903. None had occurred before his arrival and none after his departure.

Sergeant B. was a robust, healthy man of 31. His urine was slightly acid, showed slight cloudiness, but contained no albumen. No other formed elements were present. It was calculated that the urine contained two-and-a-half millions of typhoid bacilli per cubic centimetre. The strain was markedly avirulent for guinea-pigs, a fact which was in striking contrast with the severity of infections caused by it. When first isolated it would not kill guinea-pigs of 250 grms. weight in doses under a quarter of a whole agar culture. By passage, however, the lethal dose was lowered to one quarter of a loop. His serum gave an incomplete Widal reaction (1 in 50 positive in two hours, 1 in 100 negative in two hours at 37° C), and the bactericidal power of the serum was also very low. The fact that the virulence could be raised by passage through the guinea-pig suggested to Niepratschk that a similar process might take place by passage through human beings. Thus cases with only slight symptoms might give rise to infections of a severer type. There was the further possibility that the strain might undergo temporary alterations in virulence. In Niepratschk's view, however, one thing was certain, viz., that since October, 1905, the typhoid outbreaks in the artillery barracks could be traced only to this carrier. Among the other troops in Wesel and in the civil community there had been only a few cases.

In the following table are given the figures of typhoid incidence in the artillery department compared with that in other garrisons at Wesel and in the civil population :—

TYPHOID INCIDENCE PER 1,000.

——	1904.	1905.	1906.	1907.	1908.
Affected artillery detachment...	2·74	19·18	5·48	54·79	2·74
Other garrisons	0	1·07	0·53	0·26	0
Civil population	0·36	1·18	0·2	0·61	0·1

The table shows very clearly the heavy incidence of typhoid fever in the artillery detachment.

All three batteries of artillery were equally affected (1st Battery, 11 cases ; 2nd Battery, 9 cases ; 3rd Battery, 11 cases), and not Sergeant B.'s battery only. B. stated that he was in the habit of passing his urine only in the latrine. He may, however, in Niepratschk's opinion, have urinated occasionally in the stalls, so that the persons who had to change the straw or clean the stalls may readily have soiled their fingers or the soles of their boots with the typhoid bacilli. When they came to clean their boots the same danger was present. It was significant that the shoemaker who mended Sergeant B.'s boots took typhoid fever. Out of the 28 cases only two "Unteroffizieren" (the class to which Sergeant B. belonged) developed typhoid fever, and it is suggested that their immunity arose from the fact that they did not brush their own boots.

Sergeant B. was isolated for two years, and no further cases occurred in the regiment. The treatment adopted with apparent success in the case of Sergeant B. will be referred to in the chapter on urinary carriers.

The following regimental cases at Kilworth (Ireland) are reported for convenience in this chapter although the carrier in question was a civilian. The infection was transmitted by milk contaminated by the carrier. Dorgan (1910) has recently published a brief account in the Journal of the Royal Army Medical Corps, and from this I quote the following particulars :

Twenty-four cases in all occurred among the various regiments stationed at Kilworth during the period May to August, 1909, and the following table shows the dates of onset with remarks relative to the origin of the milk supplied to the respective messes affected :—

No.	Name.	Regiment.	Onset.	Remarks.
1	Captain C. ...	E. Yorks...	24.5.09	Inspector of musketry. Had tea in garrison mess about end of April.
2	Lieut. D. ...	Sherwoods	8.7.09	Lived at garrison mess. (O'Ns. milk.)
3	Pte. R. ...	Sherwoods	17.7.09	Waiter at garrison mess. (O'Ns. milk.)
4	Lieut. P. ...	S. Lancs....	12.7.09	Officers at a detached mess and used O'Ns. milk. Privates acted as waiters.
5	,, M. ...	,, ...	17.7.09	
6	Pte. C. ...	,, ...	15.7.09	
7	,, A. ...	,, ...	17.7.09	Died.
8	Capt. B. ...	R. M. F. ...	26.8.09	Regimental mess. O'Ns. milk.
9	Lieut. H. ...	R. A. M. C.	23.8.09	Garrison mess. O'Ns. milk.
10	,, W. ...	R. W. F....	24.8.09	
11	Lieut. M. ...	R. M. F. ...	28.8.09	Regimental mess. O'Ns. milk.
12	,, D. ...	,, ...	31.8.09	
13	,, S. ...	,, ...	1.9.09	
14	,, H. ...	,, ...	31.8.09	
15	,, E. ...	,, ...	1.9.09	
16	,, C. ...	,, ...	30.8.09	
17	Capt. S. ...	,, ...	3.9.09	
18	Pte. D. ...	R. M. F. ...	16.8.09	Kitchen man (officers' mess). Had been ill a few days on duty and may have infected the mess.
19	Pte. J. ...	R. M. F. ...	2.9.09	Mess waiter.
20	Pte. S. ...	R. M. F. ...	30.8.09	Regimental duty : the only case that cannot be traced to the milk.
21	Lance-Serg. S.	R. M. F. ...	23.8.09	Died.
22	Serg. B. ...		21.80.9	Sergeants' mess. O'Ns. milk.
23	Pte. G. ...	Conn. Rang.	27.8.09	Mess waiter. Admits drinking unboiled milk.
24	Child "B."...	R. E. ...	19.8.09	Visited camp and drank milk at O'Ns. farm on Aug. 10.

In all cases the milk which contrary to explicit regimental orders appeared to have been consumed in the unboiled state by the soldiers attacked came from the same farm occupied by a farmer O'N. The members of O'N's. household were examined by the Widal test and one girl, a dairymaid, was found to give a definite reaction in 1 in 100. After some difficulty, specimens of her excreta were obtained, and the B. typhosus was isolated from her urine. This woman had had enteric fever in 1903 when she was employed at this farm. Six months after her attack she returned to her duties there, when the farmer and his child were attacked. In 1906 she was employed in a similar capacity by a farmer at "G" near Kilworth. Soon after her arrival the farmer's child became ill, then the farmer himself and his wife, and also a labourer's wife and child. Two other children who had been at a boarding-school returned home on vacation, and both developed typhoid fever. On February 1st, 1909, she returned to reside at O'N's farm, but since November, 1908, she had worked there at odd times. Two sisters of O'N. died in December, 1908, of an acute fever which was since believed to have been enteric. Also a carpenter working in the camp and drinking O'N's milk contracted typhoid fever on February 7th, 1909. It was further ascertained that another married sister of O'N., who lived on a farm about a mile away was ill with enteric fever in September, 1909. There was much communication between the two houses. Also in the same month a civilian post office clerk contracted typhoid fever. O'N. supplied this post office with milk.

Including the civilian cases, this urinary carrier appears to have been responsible for about 40 cases of typhoid fever altogether.

Tsuzuki (1910) has recently reported on the occurrence of carrier cases in a division of the Japanese Army. The division in question (the XVth), which was formed during the war of 1904–5, was first attacked by typhoid fever while in Manchuria. After the war it remained in Korea till February, 1907, when its quarters were transferred to Narachino about 30 kilometres from Tokio. In October, 1908, it was transferred to Toyohashi. During 1906, 1907, and 1908 the numbers of enteric cases were respectively, 373, 211, and 64, being distributed as follows :—

Month.	1906.	1907.	1908.
January	15	1	6
February	2	2	3
March	8	1	7
April	—	—	9
May	4	1	14
June	16	1	16
July	44	32	—
August	54	67	4
September	87	87	4
October	80	11	1
November	50	8	—
December	13	—	—
Totals	373	211	64

The bacteriological examinations were carried out during the eight months, March–October, 1908, and there were examined—

(1.) All persons who had previously had typhoid.
(2.) Healthy men in companies where a new case had occurred.
(3.) Persons occupied in the kitchens.
(4.) Convalescents.

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In all 5,109 examinations were performed of 2,785 persons. The results of this investigation are detailed in Chapter II. A total of 11 carriers was discovered, viz., six who had previously had enteric, two who had no record of typhoid, and three convalescent carriers. There was, therefore, in Tsuzuki's view little doubt as to the origin of the outbreaks in this division both during the campaign in Manchuria and in their quarters in Korea. Since the carriers were discharged from the regiment, the garrison at Toyohashi has displayed a satisfactory bill of health.

CHAPTER VII.

PATHOGENESIS OF THE TYPHOID-CARRYING STATE, WITH PARTICULAR REFERENCE TO THE INTESTINAL CARRIER.

The discovery of the typhoid bacillus in cases of cholecystitis, cholelithiasis, bone abscesses, &c., long after recovery from the primary infection, was made many years previously to the recognition of the typhoid-carrier. The fact, also, that at post-mortem examinations of persons who have died of typhoid fever, the typhoid bacillus is invariably found in the bile and in the upper portion of the small intestine has been known since the work of Anton and Fütterer (1888) and later of Chiari (1894), and many others. In 1899 Droba (1899) recorded a case of cholelithiasis which was operated on, in which the B. typhosus was isolated from the gall bladder contents as also from the interior of the gall stone. The interval since the primary typhoid infection was 17 years.

Similar finds of the B. typhosus in cases of cholelithiasis at longer or shorter periods after typhoid fever were made by Miller (1898), Brion (1901), Findlay and Buchanan (1906), Simon (1907), Dudgeon (1908), and many other observers.

A definite history of a typhoid infection in these cases may be wanting. Thus Blumenthal (1904) records two cases where there was no previous history pointing to typhoid or any like infection. One of these was a woman of 37 years who did not remember having an attack of typhoid fever. At the operation the gall bladder contained two round stones, the cystic duct and the choledochus were patent, and the typhoid bacillus was recovered from the pus in the gall bladder but not from the gall stones. In this case the fæces and urine were examined and found negative. It must be remembered, however, that a single negative examination of the excreta can lead to no definite conclusion.

Though this person had never had typhoid fever according to her own story, it was ascertained that her husband died of typhoid fever, that her brother and a child of her own (10 months old) suffered from a typhoidal attack in the beginning of January, 1904, while in a house only 100 yards distant there had been five cases of typhoid fever. It seemed therefore highly probable in view of such evident association with typhoid cases, that she may have passed through an ambulant form of fever, culminating in cholelithiasis. Her serum agglutinated the homologous strain in the unusually high dilution of 1 in 2,500. Cushing's (1898) case also presented no history of enteric fever. The Widal reaction was positive, and typhoid bacilli were present in the bile.

The case reported by Finlay and Buchanan in 1906 presents points of great interest in connection with the carrier question, as it is one of the few cases in which examination of the fæces was carried out. A married female, aged 51 years, had suffered from weakness, loss of appetite, and a severe bilious attack two months before seeking advice (August, 1905). In 1880 she had had a febrile attack lasting three weeks, which was thought to be gastric fever. On examination in August, 1905, a large painless tumour was found in the region of the gall bladder. Her temperature reached 103·2° F., and during the first five days while she was under observation the temperature curve suggested that of a declining typhoid fever, but there were none of the classical signs of the disease. Her blood gave a positive Widal reaction (1 in 50 in one hour). A diagnosis of typhoidal cholecystitis was made and was supported by the discovery of typhoid bacilli in the fæces. At the operation on 15th August the gall bladder was found to be greatly distended, and a clear water fluid escaped followed by milky, and finally, purulent material. Drainage was resorted to, and from 19th August to 22nd September typhoid bacilli were constantly present in the discharge. About 30 small stones were washed out at intervals. Bacteriological examination of the discharge on the 22nd and 28th September did not reveal the presence of the typhoid bacillus. On 4th October signs of pleural effusion, breathlessness, and abdominal distension supervened, and death took place on 14th October as the result of cardiac failure. The pleural fluid was sterile. Unfortunately no post-mortem examination was made in this case, but it seems highly probable in the light of very similar cases reported of late, that this woman had been for many years a chronic carrier and had succumbed to an autoinfection. (*Vide* Chapter VIII.)

In a case reported by Dudgeon there was no history of typhoid fever. The patient had served in the Army in India and in 1900 had suffered from a severe attack of colic. No further attack took place until six months before coming to hospital (1908). Jaundice supervened and his blood gave a reaction in a dilution of 1 in 500. An operation was performed and a gall stone was removed which was sterile, but the bile contained typhoid bacilli. The fæces and urine were negative. Three weeks later the bile still showed the B. typhosus.

An acute cholecystitis may however occur at a very early period of convalescence from typhoid fever. The case reported by Gilbert and Girode (1893), is of interest from the fact that a microscopical examination was made of the gall-bladder wall. The patient was a female of 45 years, who developed a purulent cholecystitis in the fifth month of her convalescence from typhoid fever. On operation calculi were found and the typhoid bacillus was present in the pus. Sections of the bladder-wall showed accumulations of small cells in the mucosa, with masses of typhoid bacilli embedded in them.

Hilgermann (1909) gives an account of a woman (aged 29 years) who contracted tpyhoid fever on 23rd August, 1908, and whose temperature fell to normal on 24th September. Shortly afterwards a sudden attack of gall stone colic supervened and in the course of ten days a tumour developed in the gall bladder region. On 4th October, 1908, the gall bladder was extirpated. The fæces on 16th October were negative, but on 20th October, typhoid bacilli were present. Later examinations, however, were negative and she was discharged cured on 20th November. The gall bladder contained 300 c.c. of foul-smelling fluid and a stone of the size of a pea. From the pus the B. typhosus was recovered in pure culture. Histological examination of the gall-bladder wall showed disappearance of the epithelium, and inflammatory infiltrates in the submucosa and muscularis. Typhoid-like bacilli were present only in the subserosa. In Hilgermann's view the bacilli had penetrated from the inside of the gall-bladder through the epithelium into the deeper layers and so to the outer wall. One might therefore readily conceive how, with a chronically inflamed mucosa and the presence of typhoid-nests in the layers of the bladder wall, fresh infections of the gall bladder contents might periodically occur and so in some measure explain the intermittent excretion of bacilli by the fæces. The importance of a case like this lies in the fact that some light is thrown on the pathogenesis of the typhoidal cholecystitis and all such observations are of value at the present time. As we shall see a very similar condition of affairs has been found in fatal cases of enteric fever (Josef Koch (1909)) and experimentally in rabbits (Chiarolanza (1909)).

I have mentioned that the fæces contained typhoid bacilli on the 16th day after operation and thereafter were typhoid free. In connexion with treatment in Chapter X., the value of cholecystectomy as a remedy for the carrier condition will be discussed, but it may be remarked here that, in order to be certain that the patient is bacteriologically typhoid free, a much longer period of observation is necessary. The case, however, was a very early one in typhoid convalescence and, as such, it seems quite possible that a bacteriological cure was affected before chronic changes in the gall bladder and in the neighbouring parts had had time to establish themselves.

A case bearing on this point has been under observation by Theodore Thomson and the author. Mrs. B. had enteric fever in June, 1909, and was discharged from hospital on 2nd July. The last two of the three examinations of her fæces before discharge were positive but the urine was always negative. No further samples could be procured from her after her discharge. She commenced to suffer from gall stone colic in October and was admitted to St. Bartholomew's Hospital on 1st November, 1909. The stools and urine were there examined with negative results on 2nd November. On 19th November she was operated on, when a small gall bladder with thick walls and full of stones was removed. The contents of the gall bladder contained typhoid bacilli but the fæces and urine were negative.

Samples of this woman's stools and urine were examined by me on 7th December, 1909, when the fæces were found to contain typhoid bacilli. She was discharged on 15th December, 1909.

Another examination of the fæces in February, 1910, was negative. It is of great importance that a case like this should be periodically examined with a view to discovering whether a real cure has been effected. It has, however, proved impossible to obtain further samples of the woman's excreta.

Hertz and Adams (1910) have also reported a case in which a purulent cholecystitis accompanied by gall-stones intervened at an early period in convalesence from typhoid fever. The patient (female of 24 years) was admitted to the Brook Fever Hospital on 22nd December, 1909. Her temperature fell to normal on 2nd January, 1910, but a relapse occurred from 14th January to 24th January. On 1st February, 1910, she complained for the first time of pain in the epigastrium and back, accompanied by vomiting. The gall-bladder was found to be enlarged and tender. On 18th February the temperature rose to 99·4°F. and she was sent to Guy's Hospital, where she was operated on the same evening. The gall-bladder was opened and, after about 4 ozs. of colourless clear fluid had escaped, about ½ oz. of pus was evacuated along with 25 facetted cholesterol gall-stones. The B. typhosus was recovered from the pus and from the centres of some of the gall-stones. The gall-bladder was drained and the patient made a good recovery.

Since the discharge of this case from hospital I have had an opportunity of examining her excreta on two occasions, viz., 2nd April, 1910, and 13th May, 1910. On both occasions the fæces were found to contain typhoid bacilli, so that no improvement in the carrier condition can so far be recorded as the result of the operative procedures carried out.

Hitherto I have referred to the finding of the B. typhosus in persons suffering from cholelithiasis who had not previously been regarded as typhoid carriers in the sense in which the term is used in this memoir, but there can be little doubt that many of these cases would have been found to be actively or intermittently excreting the B. typhosus in the fæces had the attention of the bacteriologist or those concerned been directed to this possibility.

Before passing to the discussion of recognised typhoid carriers and their relation to gall-bladder troubles, some mention may be made of the positive Widal findings so often referred to in jaundiced patients before the carrier condition was recognised. According to Kohler (1902), who collected 614 references, which had appeared up to the spring of 1901, concerning the agglutinins in typhoid fever, the prevailing idea then was that the presence of bile elements in the blood serum influenced the agglutinating power of the latter towards the typhoid bacillus. As a matter of fact the bile itself, though it possesses in low dilutions an agglutinating effect on the typhoid bacillus, shows no greater agglutinating power over typhoid bacilli in persons dying of typhoid fever than in persons dying of other diseases.

By injecting into dogs and rabbits the various elements of the bile (taurocholic acid, &c.) or by creating artificial biliary stasis through ligature of the ductus choledochus, Kohler attempted to show that the agglutinating power of the serum towards the B. typhosus is artificially developed. For example, in one experiment before operation the serum gave no agglutination in a dilution of 1 in 10. After operation when bile pigment was present in the urine, the serum gave a slight reaction at 1 in 60, and in another case a slight reaction at 1 in 20. It cannot be admitted, however, that the figures are at all significant and further experiments by Venema (1906) showed that the addition of human bile to serum did not influence its agglutinating power towards B. typhosus or B. paratyphosus.

Carriers and Gall Stone Disease.

Quite a large number of carriers suffer from gall stones, while in others, though symptoms may have been absent, a condition of cholelithiasis has been almost invariably found, whether on examination post mortem or at operations directed towards bacteriological cure of the carrier condition. As early as 1892 Naunyn (1892) had observed that gall stone troubles frequently occurred in persons who had suffered from typhoid fever.

Forster (1908) was the first to direct attention to the association of gall bladder complaint with typhoid carriers. He found that out of a total of 194 convalescent carriers, who continued to carry the bacilli for some weeks after convalescence, 29 per cent. were men, 45 per cent. were women, and 26 per cent. were children. On the other hand out of 173 chronic carriers who continued to excrete the bacilli from 1 up to 30 years after the primary attack, 79 per cent. were women, 17 per cent. were men, and 4 per cent. were children. This striking preponderance of female chronic carriers over male (nearly 5 to 1) suggested a strong analogy to the relative gall stone incidence in the female and male, which is approximately 3 to 1. As a matter of fact 25 (*i.e.*, 14 per cent.) of the 173 chronic carriers referred to presented gall stone symptoms during life, while the remaining 86 per cent. had no such symptoms. This accords well with the known fact that 90 per cent. of all gall stone cases present no symptoms during life. Similar percentages have been obtained by other observers, *e.g.*, Mayer, G. (1910) (*vide* Chapter II.).

There has been considerable discussion as to whether the typhoid bacillus directly excites the formation of the gall stone and even forms a nucleus for it, or whether the stone is preformed and is later penetrated by the typhoid bacillus. The question cannot yet be considered as settled, but the chief arguments on either side may, with advantage be referred to here.

In the first place the typhoid bacillus has been repeatedly isolated from the centre of gall stones in cases of cholelithiasis operated on by the surgeon and in chronic carriers either at operation or at autopsy (*vide* Chapters VIII. and IX.). Individual instances of such findings need not be mentioned in detail, but I may refer here to a carrier case in which the typhoid bacillus has on two occasions been isolated from gall stones passed in the fæces. This case has been under my observation for two years. He is a medical man, and has kept accurate records of his gall stone attacks, which he has kindly placed at my disposal. The primary typhoid infection occurred in November and December, 1896, and was a very severe one with two relapses. Convalescence was established at end of February, 1897, and on August 24th of the same year he had his first attack of biliary colic which was accompanied by slight jaundice and lasted four days. Two further attacks had their commencement on November 10th and December 13th respectively. In 1898 there was only one attack commencing on January 14th and lasting five days. The patient enjoyed a respite from gall stone colic till April, 1902, when five transient paroxysms lasting each half-an-hour occurred on 5th, 11th, 14th, 16th and 20th April. No stone was passed.

On April 21st a severe attack occurred, and on this occasion a mulberry-shaped calculus weighing 4 grains and consisting of bile pigment was found in the stools.

Transient colic attacks were experienced on May 4th and June 23rd followed on July 17th by a severe attack lasting five days and accompanied by slight jaundice.

On July 27th there was a less severe attack lasting two days, and a calculus similar to the first was found.

In 1903 the first attack commenced on March 17th and lasted five days; a calculus was found. On April 11th a similar attack occurred, with passage of a calculus. There were also similar attacks lasting two days and with passage of calculus on May 12th, June 2nd, June 11th, July 3rd, August 18th, and September 15th.

1904. Attacks occurred on July 5th, 7th, and August 18th, with passage of calculi. On October 1st there was a severe attack with renewal of colic on fifth day; two calculi were passed. On November 24th an attack occurred lasting three days; a calculus was passed.

Three years of freedom intervened.

1907. On November 23rd, 24th, 28th and 30th, December 27th and 30th there were transient attacks of colic unaccompanied by passage of stone.

1908. On January 2nd occurred the severest attack yet experienced, requiring the administration of an anæsthetic; a stone was passed. On March 14th biliary colic began and lasted three days. The stone passed on this occasion was submitted to bacteriological examination (at the Lister Institute) and found to contain typhoid bacilli. From that date to the present numerous examinations have been made of his fæces and of occasional gall-stones. On March 24th he suffered from two days' illness; no stone was passed.

1909. On May 5th, 6th and 7th transient attacks occurred, each lasting half-an-hour. Later, on the 7th, a severe attack ensued lasting three days, and accompanied by passage of a stone. On October 3rd prodromal colicky pains began at 11 a.m. and severe colic at 9 p.m., which entailed confinement in bed till 6th October; a calculus was passed.

This last calculus, which was passed on 6th October, 1909, was placed on cotton-wool in a pill box, and was not handed over for bacteriological examination until 3rd November, 1909. It was a brown friable pigment stone of the size of a large pea. Owing to its rough friable and porous character, it was impossible to sterilise the exterior thoroughly. Accordingly it was shaken in a tube of sterile broth, removed, dipped in alcohol and flamed two or three times, and finally ground up in a mortar containing a small quantity of sterile broth. The washings and the stone emulsion were then immediately plated on bile-salt-lactose-agar. Next day the plates contained enormous numbers of typhoid bacilli in pure culture. The strain was agglutinated by an antiserum in dilution of 1 in 7,000, and was lethal for a guinea-pig of 250 grms. weight (intraperitoneal injection) in 0·5 c.c. of a 48-hours broth culture. That the typhoid bacillus would be viable in a gall-stone after a month's sojourn in cotton wool was not anticipated, and in view of the positive result two gall-stones, passed by the same patient on 9th May, 1909, and 29th December, 1907, respectively, were examined in a similar way on 5th November, 1909. Neither, however, contained typhoid bacilli. Kramer (1907) had also observed that typhoid bacilli contained in apparently dried up bile salts retained their vitality for a considerable time.

At the close of Chapter XII. will be found details concerning the bacteriological examination of the excreta of the above case (P.).

A case in many respects similar to the above was reported by Dean (1908). The carrier, who was also a medical practitioner, had passed through a severe attack of enteric fever 29 years previously. Within three months of his illness he had an attack of acute pain in the gall-bladder region, and for more than a year thereafter he suffered from biliary crises at intervals of about three months. Jaundice was occasionally a feature of these attacks. Afterwards, however, the attacks became less frequent (one or two per annum), and they have never led to any interference with his medical work. His fæces showed on examination (in spring of 1908) enormous numbers of typhoid bacilli, but the urine was negative. His serum gave a negative Widal reaction. Since 1908 numerous examinations of his fæces have been made with, as a rule, positive results. Neither of the above two cases is known to have caused infection in other persons.

Bacmeister (1907) reported the bacteriological examination of a series of 20 gall-stones from various cases. Of these 16 were sterile and four contained bacilli in the centre, viz., B. coli (two cases) and B. typhosus (two cases). One of these latter was a female who died of typhoid fever in the fourth week of the disease. There was no evidence in this case of a previous attack of typhoid fever, and he considered it very unlikely that in three weeks the typhoid bacillus could cause the formation of a hard stone of the size of a cherry, although Mignot (1898), Droba (1899), Naunyn (1892), believed such rapid formation possible. Hertz and Adams (1910) calculated that, in their case reported above, the gall-stones must have taken less than 68 days—probably not more than 50 days to form. The evidence they assign, however, is not indisputable as, although there was no history of an earlier typhoid infection, the authors explicitly state that the patient had occasionally suffered from a dull aching epigastric pain since the birth of her only child three years ago. In Bacmeister's view stones found in recent cases of cholecystitis were as a rule sterile, while organisms were only to be found in old stones into which they had penetrated. The opposite view has been held by other observers, *e.g.*, Cushing, viz., that only recently formed stones contain bacilli. Gilbert and Fournier (1896) had previously experimented with gall-stones and broth cultures of B. coli and found that the bacilli wandered in when the stones were of cholesterin, but not in the case of other stones. Their experiments were repeated by Bacmeister, who placed gall-stones in both broth and bile cultures of B. typhosus. Most of the stones remained sterile, but in two cases (after eight days and 24 days respectively) the B. typhosus was recovered from the centre of the stone. One of these stones was a mulberry cholesterin stone of the size of a hazel-nut while the other was a facetted stone of the size of a cherry. They had been obtained from two women of 38 years and 82 years of age respectively. It may be noted that no mention is made of the history of these women or of the interval between the experiment and the obtaining of the stones. The possibility is not excluded that these cases had been carriers, and the typhoid bacilli may still have been viable in the stone as in the case referred to above.

The fact that bacilli can penetrate into the interior of gall-stones is a point of great importance, but it by no means follows that in the genesis of gall-stones micro-organisms play an entirely passive role. The experiments of Gérard (1905), Kramer (1907), Bacmeister (1908) and others go to show that embryonic gall-stone formation may be observed in test-tubes containing bile cultures of B. typhosus, B. coli, and other micro-organisms. The last-named observer found that B. coli and B. typhosus, B. proteus, and especially B. pyocyaneus could cause a precipitation of cholesterin from filtered bile. True concretions were also found after prolonged growth on this medium. Their ability to produce such precipitates was much enhanced by employing unfiltered bile containing epithelial elements. Similar precipitates of cholesterin also occurred in sterile filtered bile in which no micro-organisms had grown, so that in the genesis of the pure cholesterin stone, at least, stasis alone can act as the exciting factor. The presence of epithelial elements or bacteria in the test-tube experiments, merely accelerated and intensified this precipitation of cholesterin. For the genesis of the mixed cholesterin-chalk stone, however, they believed that a chronic inflammatory condition of the bladder wall was essential. Exner and Heyrovsky (1908) performed similar experiments with ox bile and human bile and also with broth to which the bile salts were added. They found that some micro-organisms, especially those of the typhoid-group, could readily break down the bile salts (sodium glycocholate and sodium taurocholate), thus causing a precipitate of cholesterin. In this reaction they believed that the soaps and fatty acids of the bile played no part. They found, indeed, that the bile contained only a very small proportion of true fatty acids.

In the light of these experimental results there would seem to be no doubt that the typhoid bacillus may play a part in the formation of gall-stones, but at present we are unable to say how far this formation is contributed to by other factors.

Our knowledge of the relationships of B. typhosus to the gall-bladder has been considerably enhanced by animal experimentation. So long ago as 1899, Blachstein (1899) and Welch (1899) in America demonstrated that in rabbits which had been inoculated intravenously by typhoid bacilli the gall bladder might continue to harbour these organisms for a very long period, even up to 109 days.

Forster and Kayser (1905), the former of whom, as I have already noted, put forward the view that the gall bladder was most probably the seat of vegetation of the typhoid bacillus in carriers, repeated the experiments of Blachstein and Welch with a view to reproducing the carrier-state in the rabbit. They also found that after large doses given intravenously the bile might still be infective six weeks later. Typhoid bacilli could also be recovered in some cases from the upper intestine. Further, they made the important observation that in cases in which the bile was sterile the typhoid bacillus could occasionally be isolated from the gall bladder mucosa. Similarly in man at a very early stage in the disease the bacilli would reach the gall bladder and there set up definite lesions which might or might not be accompanied by distinctive clinical symptoms. According to Forster and Kayser the bacilli would reach the liver by the blood, be excreted by the bile and so reach the gall bladder.

In the same year Doerr (1905) recorded the results of experiments undertaken to test whether the typhoid bacilli reached the gall bladder by the downward route from the liver through the blood, or by the upward route from the intestine. They showed that bacilli appeared in the gall bladder as early as eight hours after intravenous inoculation. When, however, the hepatic duct was ligatured the bile invariably remained sterile. Also when the cystic duct was ligatured no bacilli could be demonstrated in the bile, thus proving that the bacilli travelled by the bile and not by the blood vessels of the gall bladder itself. These latter experimental results dealing with ligature of the cystic duct have recently been called in question by Koch, J. (1909), and Chiarolanza (1909). The former (at the instigation of Frosch, who believed that not only the gall bladder, but also the biliary tracts and perhaps the liver itself were seats of vegetation of the typhoid bacillus in carriers) investigated the histology of the gall bladder mucosa in a fatal case of typhoid fever. The patient had died of heart failure in the third week of the disease.

The organ contained cloudy, slimy, green bile, and its walls were much thicker than normal. No stones were present. Typhoid bacilli were recovered from the gall bladder wall, the larger biliary tracts, the mesenteric glands, renal pelvis, and small intestine, but not from the heart blood. On microscopical examination the mucosa of the gall bladder was very much corrugated and papillated, and, near the extremities of the papillæ, typhoid nests were found with necrotic areas in their vicinity. The superficial epithelium had completely disappeared and there was a marked inflammatory proliferation of the sub-mucosal folds. A conspicuous feature was the close relationship of these typhoid nests to the minute end-capillaries of the sub-mucosal papillæ, suggesting that the bacilli had reached this situation solely by way of the blood vessels. No organisms were demonstrable microscopically in the lumen. The experiments of Chiarolanza entirely supported this view. Even within two hours of intravenous injection, typhoid bacilli were recovered from the gall bladder wall. Also, contrary to Doerr's results, bacilli were got from the gall bladder when the cystic duct was ligatured. The histology of the rabbit's gall bladder was essentially similar to that of the human case above referred to. The walls were thickened and infiltrated and the sub-mucosa very cellular with papillary proliferations containing typhoid nests at their extremities. Sections of the bile tracts and the intestine showed parallel changes, and there was a marked small-cell proliferation in the portal areas of the liver itself. It would appear, therefore, that the main, if not the only route, of the typhoid bacilli to the gall bladder is by the vessels of that organ itself. In any case this is the chief route to be considered in drawing deductions as to the possible value of surgical interference with the gall bladder as a remedy for the carrier-state. The bacilli vegetate in these sub-mucosal nests and not in the bile itself. The latter passively receives accessions of typhoid bacilli from ruptured nests either in the bladder mucosa or in the biliary tracts. I shall further discuss the bearing of these facts in a later chapter (*vide* Chapter IX.).

I shall conclude this section with certain general considerations which have been put forward in explanation of the carrier state. In the first place with regard to the preponderance of cholelithiasis in the female, various reasons have been assigned, such as the wearing of tight corsets, frequent pregnancies, &c., causing portal stasis.

Similar factors may, however, according to Forster, play a part in rendering males liable to carry the bacillus indefinitely after the primary attack. Thus Forster (1908) mentions the case of a man who contracted typhoid fever two years after an operation for appendicitis. After his recovery his wife took typhoid fever and the husband was then found to be a carrier.

Owing to the appendix operation and ensuing inflammation anatomical changes had taken place in the peritoneum, thus altering the circulatory conditions and probably predisposing to the carrier state. This explanation by Forster may have some foundation in fact, but further data must be awaited before one can draw any definite conclusions on this point. One may note, however, that Lentz (1905) had already suggested that the greater liability of women to become carriers probably bore some relation to the circulatory disturbances incidental to pregnancies and to over-exertion in household duties.

An interesting view lately put forward by Prigge (1909) in order to explain the higher proportion of women carriers may also be noted here. Whereas, according to Prigge, the incidence of enteric fever on females reaches a maximum between the ages of 15 and 20 years, the probability that a woman will become a chronic carrier increases gradually from the 15th to the 45th year. This fact suggested to him the possibility that predisposition to the carrier state might be induced by the menstrual and puerperal blood losses. There is some evidence that these physiological crises are accompanied by a diminution of the alexin-content of the blood serum, which would render the subject for the time being more vulnerable to an infecting micro-organism. In support of this view it is alleged that enteric fever (often mistakenly diagnosed as puerperal fever) is of frequent occurrence at childbed. If to the general blood changes at these seasons there be added the pressure caused by a gravid uterus on the biliary system, there would, it is maintained, be a sufficiency of factors predisposing to the carrier state. As Bacmeister showed in his in vitro experiments, stasis fluids accelerate the precipitation of cholesterin by bacteria. If therefore a woman who has previously had an attack of cholecystitis contracts enteric fever, the chances of her remaining a carrier after her attack would be intensified.

Fornet (1909) has recently formulated the view that the carrier state is to be regarded as a consequence of established immunity to the typhoid bacillus, and that, in fact, the bacilli discharged by the carrier may not necessarily be descended from those which caused the primary infection. A re-infection takes place which, according to Fornet, is not accompanied by any clinical symptoms. The region attacked by the bacilli in this re-invasion, would have acquired, in consequence of the primary attack, such a tolerance to the micro-organism as to render its saprophytic existence possible.

This view was based by Fornet on the following considerations:—

Klinger had found for the year 1907 of the typhoid campaign a carrier output of only ·9 per cent., whereas most individual observers have obtained a much higher percentage (*see* Chapter II.). Fornet thinks, therefore, that persons may not become carriers as the result of the primary infection, but only after a second symptomless infection. The carrier statistics for the year 1908 (compiled by Fornet) are adduced in support of his view. Thus, in that year, 91 carriers (temporary and chronic) were discovered in the course of the typhoid investigations, and, as Klinger had already noted in his series (Chapter II.), the group of chronic carriers was almost exclusively made up of adults, whereas among the temporary carriers children formed a large contingent (30 per cent.). Fornet argues that, as the adult has probably had more opportunities of having passed through an attack of typhoid fever than the child, the prospect of his becoming a carrier as the result of a second infection would be correspondingly greater. Accordingly, if his view that the carrier state is the culmination of a symptomless re-infection be a correct one, he would expect to find among the chronic carriers of the year 1908 a greater proportion of adults who had already had typhoid than of adults who had not so far suffered from the disease. As a matter of fact 59 per cent. of the chronic carriers had already had typhoid, while 41 per cent. had not yet had the infection. Among the temporary carriers, on the other hand, 74 per cent. had not yet had the disease, while 26 per cent. had recovered from a primary attack.

It does not appear to me valid to employ these statistics in this way, in view of the difficulty of determining whether a person who happens to be a temporary carrier has really passed through a typhoid infection or not. While recognising the important distinctions that separate the two groups of chronic and temporary carriers particularly in the matter of age and sex, it would be unjustifiable in the present state of our knowledge to lay stress on the numerical distinctions between the carriers in each group who have had a previous infection and those who have not. Indeed, from Klinger's collected statistics up to 1907 (*see* Chapter II.) it is seen that 80 per cent. of the carriers had had a primary infection, while 20 per cent. had not. Of the temporary carriers 43·6 per cent. had had a primary infection, while

56·4 per cent. had not. Thus the relative percentages in this latter group differ considerably from those of Fornet for the year 1908.

Finally, in view of the gradual accumulation of cases which have been traced bacteriologically from the convalescent stage onwards to the chronic carrier state, such a theory as that of Fornet would seem to me at present uncalled for. It is undoubtedly, however, an interesting speculation, and it remains to be seen what amount of support is lent to it by the results of experimentation on the saprophytic growth of pathogenic bacteria in the immune organism.

CHAPTER VIII.

PHYSICAL DISABILITIES OF THE CARRIER STATE, AUTO-INFECTION, &C.

The question is frequently asked whether the typhoid carrier suffers in bodily health as the result of the carrier state, or whether *ceteris paribus* he or she remains a normal healthy individual. In general it may be said that the carrier who has no definite gall bladder symptoms is little if at all inconvenienced in bodily health by the fact that the typhoid bacillus has acquired a permanent habitat in some portion or portions of his anatomy. Occasionally headaches are complained of, particularly by urinary carriers, and measures taken to arrest the typhuria have reacted favourably on the general well-being of these cases.

Mayer, G. (1910), however, has laid stress on the fact that certain carriers of the intermittent type have been observed to suffer from periodic intestinal disturbances after the primary infection. He states that these are specially likely to occur at certain seasons, *e.g.*, in midsummer, when winter merges into spring, autumn into winter, and that at such seasons it is advisable to exercise strict bacteriological supervision over declared carriers. Also it must be admitted that in persons of nervous temperament who are aware of their condition there is good evidence that the knowledge of their having caused disease in other persons, the consequent anxiety and the necessarily harassing precautions to be taken with regard to disinfection, &c., develops a form of neurosis which may react injuriously on the general bodily health. Such cases have not infrequently been met with, and the fact that the carrying-state may have this unfortunate and serious issue calls for the greatest tact on the part of those whose duty it is to exercise supervision over carriers.

In this section I propose to discuss mainly those cases in which a recognised carrier suddenly develops a train of symptoms pointing to a general infection by the bacillus he or she is carrying. Only a few examples have so far been reported in which an auto-infection has been indicated, but they are of such importance for an understanding of the carrier-state, that they will be referred to in some detail.

The first of such cases was recorded by Levy and Kayser in 1907. The patient (female, aged 35 years) was an inmate of the Hordt Asylum, an institution in which 13 other carriers were discovered at various times (1904–5). She was admitted to the Asylum as an epileptic on 25th March, 1903. During April and May of the same year she suffered from a remittent fever, which was diagnosed as typhoid fever although no Widal or other bacteriological test was made. Two years later when carriers were being sought for to explain the typhoid epidemics in the asylum, this woman was found to be a carrier (16th October, 1905). Further examinations of her stools on 24th November, 1905, 25th January, 1906, 6th February, 1906, 2nd March, 9th April, 27th April, 28th May, 11th June, and 29th June, 1906, were positive, while the urine remained negative. On 17th October, 1905, she had been isolated along with the other carriers and a year later (8th October, 1906) she became ill with pain in the stomach region and constipation. On 12th October she was put to bed and death took place on the 18th, following a febrile attack associated with severe pulmonary symptoms. The autopsy (19th October) revealed hypostatic pneumonia of the right lower lobe and a slightly enlarged spleen. The brain appeared normal. The gall bladder contained a cholesterin stone of the size of a bean. Its peripheral layers were sterile but from the centre the B. typhosus was recovered. This bacillus was also isolated from the liver-blood, the spleen, the bile and gall bladder wall. Though the postmortem examination was performed 19 hours after death, the bacteriological results, particularly the finding of typhoid bacilli in the spleen and liver-blood and the absence of other micro-organisms led to the conclusion that the carrier had succumbed to a general infection by her own bacillus. The ill-defined pains in the stomach region on 8th October, 1906, might very well fit in with gall-bladder trouble, as it is well known (Naunyn, 1892, Riedel, 1905) that pain arising from disturbance of the latter organ may be referred to the stomach region. The discovery of the bacillus in the centre of the stone was naturally held by Levy and Kayser to give strong support to Forster's view that the gall bladder is the seat of vegetation of the typhoid bacillus in carriers.

The second case reported by Grimme (1907) as one of auto-infection will be referred to here, though the actual bacteriological proof that the woman had been a chronic carrier was wanting. The patient (aged 52 years) was also an inmate of an asylum. Suddenly when at work she developed epileptiform convulsions and became unconscious. Her temperature was 38 °C. and there was slight splenic enlargement. Vomiting occurred while the patient was being examined. On the second day, jaundice developed and the liver and spleen increased in size. There was no rash. On the third day a Widal test was positive (1 in 800) and the B. typhosus was got from the blood and fæces. Death occurred on the twelfth day. At the autopsy a cancer of the gall bladder was found which had led to the closure of the ducts and so to jaundice. One gall stone was present but the typhoid bacillus was not recovered from it. The spleen, bile and peritoneal exudate, however, contained typhoid bacilli. Peyer's patches were not swollen but appeared atrophic with bluish pigmented patches in them like the remains of some previous pathological condition. That the patient had had typhoid fever previously was rendered probable from the fact that in 1904 when outside the institution she had suffered from a febrile attack with diarrhœa, slight splenomegaly and a doubtful rash.

A very similar case, affecting also a female lunatic (64 years of age), is reported by Kamm (1909). This woman in November, 1901, passed through a typical attack of enteric fever. On 12th March, 1906, in the course of a systematic examination of the female inmates, she was discovered to be a carrier. Positive results were obtained from her stools on 8th and 20th March, 9th and 27th April, 25th May, 2nd, 12th and 20th June, 28th July, 8th and 14th August, 19th October, and 9th December, 1906, but the urine was invariably free from typhoid bacilli. In spite of all therapeutic efforts to free the patient of her typhoid bacilli, 72 out of the 85 examinations of her stools during 1907 were positive. In February–March, 1908, pulmonary troubles pointing to phthisis intervened and tubercle bacilli were found in the sputum. Death occurred on 16th March, 1908, after an attack of cerebral apoplexy lasting four days. The autopsy revealed carcinoma of the gall bladder encroaching on the liver, cholelithiasis, secondary growths in liver, pleuræ, lungs, and retroperitoneal glands. The ductus choledochus and ductus hepaticus were normal. The cystic duct was thickened and its lumen so narrowed that a sound could not be passed through the opening into the choledochus. The gall bladder was much dilated and contained 195 polyhedral stones of which the largest weighed 18 grammes. The spleen was enlarged but not the mesenteric glands. From the gall bladder, the biliary tracts, the interior of the large stone, the right and left lobes of the liver, the lungs, bone marrow, and spleen and all portions of the intestinal tract, the typhoid bacillus was recovered. It was not present, however, in the heart blood, the small stones, or the cervical mesenteric and retroperitoneal glands. How far this general infection by the typhoid bacillus had contributed to the patient's death it was impossible to say. The author refused to consider that the typhoid bacillus had merely invaded a weakened organism for the reason that, in another case observed by him (*vide* Chapter IX.), where the bodily enfeeblement was equally great, there was no general distribution of the typhoid bacilli. With the view of throwing some light on the matter Kamm made an interesting experiment which may be quoted here. Under an anæsthetic he introduced a piece of pumice stone (of the size of a pea) saturated with a broth culture of the typhoid bacillus into the gall bladder of a rabbit (16th December, 1907). The bladder was then sewn up and the animal quickly recovered. Repeated examination of the blood after the operation showed that no invasion of the blood stream by the typhoid bacillus had taken place during the operative procedures. Judging that the animal would still be carrying the bacillus at a period of three weeks after the operation, he selected uranium nitrate as a substance calculated on injection to produce an extremely weakening effect upon the animal. On the 20th, 21st, 22nd and 23rd days, therefore, after the operation, 1 c.c. of a 5 per cent. solution of this substance was injected. Extreme emaciation resulted, followed by death five days after the commencement of this treatment. At the autopsy the kidneys showed parenchymatous nephritis, but the typhoid bacillus was not recovered from the blood, spleen or kidneys. It was, however, isolated from the bile, the pumice stone, the duodenum, ileum and mesenteric glands. Thus the uranium nitrate did not lead to a general invasion by the typhoid bacillus and the problem has to be left undecided. Further experimental work on these lines is desirable as there has been a tendency in recent years to attach a perhaps unwarrantable degree of importance to those bacillary invasions which have been found to occur in mentally enfeebled persons.

The instances I have mentioned so far have all been fatal cases in which the auto-infection was verified by extensive bacteriological examinations made after death. The literature of this subject also contains not a few examples of typhoid relapses in typhoid carriers which did not lead to a fatal issue.

Davies and Walker Hall (1908) record that Mrs. H., the Brentry carrier discovered by them, developed a febrile attack on 21st May, 1908, which lasted about three weeks. No gall-stones were found in the fæces, and there were no clinical signs of biliary obstruction. It seems doubtful whether this illness was a genuine auto-infection (enteritis or cholecystitis). The agglutinins remained stationary and typhoid bacilli could not be isolated from the blood.

Mayer (1910), in the course of his typhoid investigations in the Bavarian Pfalz, gives a series of such cases which are of considerable interest, inasmuch as the carriers affected were generally intermittent carriers. After the primary attack of typhoid fever the bacilli could be demonstrated only at intervals in the fæces. With the onset of the relapse the excretion of typhoid bacilli became again a prominent feature. There was evidence too, that the Widal reaction, which may have been negative after the primary attack (though the person was still excreting the bacilli intermittently), became positive during the relapse to disappear again after recovery. In Niven's case, referred to in Chapter III., there had been a similar variation in the Widal reaction ; but there was little or no increase in the agglutinating power of the serum, either during or after the above-mentioned illness of Mrs. H. the Brentry carrier.

An interesting case of acute abdominal infection in a typhoid carrier has recently been reported by Gardner (1910). The patient (male, aged 56 years) had an attack of typhoid fever in 1906, when he was in bed for 10 weeks. In 1900 he had suffered from peripheral neuritis which was attributed to the presence of arsenic or lead in the beer "of which he drank a good deal at that time." The illness reported by Dr. Gardner commenced on 26th January, 1910, with pain in the abdomen and nausea, and lasted about a fortnight, the symptoms throughout being those of an acute cholecystitis. There was only very slight icterus, but the fæces after a calomel purge were "semi-solid homogeneous slaty-grey and very offensive." No bacteriological examination of the stools was made until the occurrence of two cases of typhoid fever in the patient's household shortly after his recovery, suggested the possibility that this man might be a typhoid carrier. This proved to be the case. His serum gave a positive Widal reaction, and his fæces were examined by me on 4th April, 1910 with positive results.

Further examinations :—21st April, 1910, positive. 7th May, 1910, negative. 19th May, 1910, negative. The urine was always negative.

Mention must also be made of the possibility of infection of the foetus in pregnant carriers either as the result of a blood invasion by the bacillus consequent on the disturbances during pregnancy and child-bed, or more probably in consequence of an actual cholecystitis during child-bed, as in a case reported by Mayer (1910), where the child was born with typhoid fever. In a later chapter (Chapter XII.) I shall refer to the successful isolation of the typhoid bacillus from the blood of the umbilical cord, at the confinement of a carrier who has been under bacteriological observation for a considerable time. The child, so far as I am aware, was quite healthy at birth.

CHAPTER IX.

TREATMENT OF TYPHOID-CARRIERS.

Intestinal Cases.

Forster (1908) has stated that if we can cure carriers we can get rid of typhoid fever, and, indeed, it may be that only time and further experience are necessary to establish the truth of this dictum. Unfortunately, it must be admitted that hitherto, no certain method has been devised of rendering carriers typhoid-free. That cases have occurred in which the excretion of typhoid bacilli has ceased spontaneously is undoubtedly true, the cessation, perhaps, coinciding with a healing of the gall-bladder trouble. It has even been noticed, as in a case reported by Forster (1908), that the excretion stopped after an acute attack of gall-stone colic which was the first that this female carrier had experienced. We cannot exercise too much caution in accepting these spontaneous cures, as it has been repeatedly demonstrated that an intermittent period may extend over many months, and further it must be remembered that our bacteriological methods are not yet sufficiently delicate to detect minimal quantities of typhoid bacilli in excreta. As an illustration of the necessity for caution in interpreting these so-called cures in temporary carriers, I may quote a personal experience. Mrs. C. had enteric fever in July–August, 1908, and her temperature had fallen to normal on the 24th of the latter month. In late convalescence she suffered from gall-stone complaint. On

30th October, her fæces were examined and found to contain typhoid bacilli. A positive result was also obtained on 8th December, 1908, but further examinations in January, March, April, May, July and August of 1909, were negative and accordingly this case was considered to have belonged to the category of temporary carriers. In January, 1910, however, another examination of her stools revealed enormous numbers of typhoid bacilli, so that the woman is to be regarded in future as a chronic carrier (*see* Table at close of Chapter XII.).

With a view to determining whether spontaneous cures occurred, Prigge (1910) made monthly examinations in the course of the last three years of his chronic and transitory carriers, with the result that of 28 chronic female carriers that had excreted typhoid bacilli over a year, one only could be struck off the list. However, in a foot-note to his paper he mentions that this woman was again excreting typhoid bacilli in October, 1909, after three years intermittence.

In other cases he noted intermittent periods extending from one to two-and-a-half years.

The drug treatment of intestinal carriers has been entirely ineffective in ridding these persons of their typhoid bacilli. Salol, beta-naphthol, calomel, bile and its salts, turpentine oil, sodium bicarbonate in large doses, chloroform, &c., have been employed with no effect or only a temporary one on the excretion of the bacilli. Recently, Hilgermann (1909-*b*) has reported what he regards as a conspicuous success in at least one chronic carrier, after prolonged treatment with sodium salicylate. The carrier was a female lunatic of 71 years. During the period from 30th September, 1905, to 31st October, 1907, her stools had been examined 19 times (*i.e.*, on an average ·73 times a month) and on 18 of these occasions they had been positive. Treatment by sodium salicylate was begun on 11th November, 1907. From this date to 11th December, 1907 she received 3 grams per day (or 45 grs. in 15 gr. doses t.d.s.).

From 12th December, 1907, to 11th February, 1908, 4 gms. per day.
„ 12th February, 1908, to 18th March, 1908, 5 gms. „
„ 4th November, 1908, to 11th November, 1908, 6 gms. „
„ 11th November, 1908, to 20th November, 1908, 5 gms. „

The result was that during the period 16th November, 1907, to 5th May, 1908, the stools were positive in 10 out of 11 examinations (32 up to 6th July, 1909), or three times monthly, were negative.

The intermittence is certainly a striking one, but without more prolonged observation one cannot regard this case as cured. Two other female carriers received similar intensive treatment with sodium salicylate without showing any marked improvement. It may be noted that 5 gms. per day (or 15 grs. five times a day) were well tolerated, but higher doses caused general disturbances.

So far as the results of drug treatment are concerned all that one can conclude at present is that internal antiseptics may, if pushed to their physiological limits, offer some slight prospect of success. Our knowledge of the pathology of the carrier state makes it difficult to conceive that any treatment other than an intensive one should exercise the slightest effect on indolent typhoidal lesions in the gall-bladder and bile tracts.

The administration of milk soured with lactic acid bacilli has been vaunted by some observers as affording an apparently permanent cure. Thus Liefmann (1909) gave Yoghurt in quantities of one-third to two-thirds litre daily to two female asylum carriers, and observed that one week after the commencement of the treatment the stools in both cases were negative. After seven weeks the stools of one of the cases were again positive, but later examinations were negative. The last examination (there were only eight in all in each case) was made at the end of the eleventh week. Evidence derived from such a short period of observation proves nothing, not even that the temporary cessation was attributable to the treatment employed.

Three asylum carriers (Thomson and Ledingham (1910)), who have been under bacteriological supervision since the latter part of 1907, received sour milk (half-a-pint three times a day) daily during the period February–December, 1909, without any appreciable effect on the excretion of typhoid bacilli in the fæces during the administration of the milk.

Captain Fawcus, of the Army Medical Department (1909–1910), has recently reported fully on the treatment of army carriers by lactic acid bacilli. Two carriers received a course of Bulgarian bacilli grown in diluted malt extract, commencing with a dose of 25 cub. cent. of the culture. No improvement whatever took place in one case except a temporary diminution in the numbers of bacilli excreted, after administration of the doses. The second case, however, reacted more favourably to the treatment. The course was commenced on 8th March with a dose of 25 c.c., and was continued till 28th May when 250 c.c. were being given daily. On 29th April the fæces were apparently typhoid-free, and from that date they remained so. The man was discharged to duty on 23rd July having been free from typhoid bacilli for three months. Further data with regard to this case will be awaited with interest.

At Netley, Major Cummins (1910) had no success with this method of treating intestinal carriers.

I now come to consider those attempts which have been made to abolish the carrier-state by surgical interference with the gall-bladder. Naturally when the view was put forward that the gall-bladder is the main seat of vegetation of the typhoid bacillus in intestinal carriers, operative interference directed towards improvement of the gall-bladder condition, suggested itself as a possible remedy for the carrier-state. The findings at such operations and at post-mortem examinations, which in some instances subsequently took place, are of much interest. I therefore propose to refer in some detail to all those cases which have been treated surgically.

Dehler (1907) operated on two female asylum carriers who had given rise to four cases of typhoid fever, including one fatal case.

Case 1 (aged 46 years) presented no history of having passed through an attack of enteric fever. Her fæces were regularly examined every three weeks, and, in 37 out of the 39 examinations made, typhoid bacilli were present. They were not found in the urine or blood. Her blood serum gave an agglutination reaction of 1 in 50, and often 1 in 100. There were no symptoms pointing to gall-bladder trouble.

On August 20th, 1906, an operation was performed. The gall-bladder was released from surrounding adhesions and opened. Two cherry-sized stones were removed, one of which had dilated the cystic duct. Typhoid bacilli were present in the bile but not in the stones. Drainage was then carried out through a tube led into the dilated cystic duct. The bile regularly contained typhoid bacilli up to the 21st day. It then remained negative until 11th October, 1906, when it was again positive. After the cystic duct could no longer be opened owning to cicatrical formation in the depth, the secretion from the fistula ceased to contain B. typhosus. The fistula cicatrised completely about the middle of December.

Three days before the operation, typhoid bacilli were found in the fæces. Subsequent to the operation 26 samples of fæces were examined in the period, 24th August–17th October, and 50 samples between 17th October and 19th February, 1907, and all were negative. The urine remained typhoid free, and the agglutinins also remained at the same titre as before the operation. Dehler noted that so long as the bile flowed freely and speedily from the fistula, the B. typhosus was scarce and was indeed for four weeks not demonstrable in the bile, but that, as the fistula narrowed and the bile flowed more slowly, the typhoid bacilli got time to propagate in the bile and were therefore very numerous.

Later still, as the fistula closed and the gall-bladder cicatrised, the bacilli disappeared as there was no further opportunity of vegetating in stagnant bile. The fact that the fæces remained negative suggested that any bacilli carried down directly from the bile paths into the intestine were overgrown by other bacteria. Also it was considered not improbable that the discharge of the bacilli from individual portions of the liver and their bile tracts would gradually cease completely. To hasten this action, cholagogues, such as calomel, &c., were given for two months.

In a later communication (22nd October, 1907) Dehler (1907) notes with reference to the above case, that on three occasions out of 176, typhoid bacilli were got in small numbers in the fæces, but believed that these few positive results might be explained by accidental mixing up of samples from other carriers. Up to February, 1907 the agglutination titre remained at 1 in 100, in March and April it fell to 1 in 50, and during May, June, and July it was quite negative. The patient remained in excellent health and the symptoms of intestinal catarrh, from which she had previously suffered, disappeared.

Case 2 (aged 45 years) had no record of typhoid fever, though she had an illness 19 years previously which might possibly have been an anomalous attack of this disease. In July, 1904, her serum had given a positive Widal reactiion, but it was not till 3rd January, 1905, that typhoid bacilli were demonstrated in her fæces. During 1905, nine samples of fæces out of 16 were positive, and during 1906, five out of 10. The urine was always negative. From

January to 9th April, 1907, 16 samples were positive out of 20, and two urine samples were positive out of 14. No gall-bladder symptoms were present during the last three years. Internal remedies had been tried with no result. On 10th April, 1907, the gall-bladder was opened and found to contain several small stones which were sterile. The bile was clear and contained numerous Bac. coli and moderately numerous typhoid bacilli. Drainage was carried out as in the last case.

The bile that drained away during the first few days after operation contained typhoid bacilli, and these disappeared as the bile flow diminished. After the 9th day from the date of the operation they were found only on two occasions in the fæces, viz., 25th May and 3rd July, 1907 (out of 30 samples). Of these 30 samples of fæces, 28 were negative ; the blood and urine remained always negative. The agglutination titre on 31st July, 1907, was positive in 1 in 100, but on 16th August, 1907, a negative reaction was obtained.

In the foregoing instances the surgical interference was confined to drainage of the gall-bladder ; in those that follow removal of the gall-bladder was resorted to.

Grimme (1908) reported that he had had the operation of cholecystectomy performed in a female asylum carrier in a Göttingen asylum. She had never shown symptoms pointing to implication of the gall-bladder.

At the operation (performed by Braun) numerous small stones of the size of peas (30–40) were found in the gall-bladder. No inflammatory changes were present, but the bile and also the interior of the stones contained typhoid bacilli. The gall-bladder wall did not contain them. Fifteen days after operation the B. typhosus was found in the fæces, but not at a later period. The period of observation, however, was only 55 days, as the patient had to be discharged from the asylum.

Loele (1909) reports the next case, also a female lunatic, aged 51 years. This woman had typhoid fever during October and November, 1908, but during convalescence no typhoid bacilli were demonstrated in the fæces.

At Christmas, 1908, she had an attack of gallstone colic with jaundice, and the fæces were now positive. There was a palpable tumour in the gall-bladder region. Her serum gave a reaction of 1 to 2,000, but the blood and urine were sterile. An operation was carried out on 16th February, 1909. The gall-bladder was very adherent and difficult to remove. Between it and the stomach was an abscess containing a stone. During the operation the duodenum was perforated. The cystic duct was quite stenosed. The hepatic duct was drained and the laparotomy wound closed except for the drainage tube and plug.

On 17th February a large flow of bile occurred, and on following days the contents of stomach and duodenum appeared with the bile. Death took place on 20th February. The gall-bladder contained pus and 21 stones of the size of hazel-nuts. The bacteriological results in this case are of great interest.

The gall-bladder pus contained typhoid bacilli, as also did the gall-bladder wall. On the first day after operation the bile contained numerous typhoid bacilli. On the third day the fæces also contained a few typhoid bacilli. The gall-stones were found to be sterile internally.

At the autopsy cicatrices of typhoid ulcers were found in the small and large intestine and bacteriological examination revealed typhoid bacilli in the following situations: small intestine (upper, middle and lower portions), transverse colon, liver, spleen, and heart blood. The urine was negative.

Loele concludes that the typhoid bacilli in the fæces did not come from the gall-bladder for the following reasons. The gall-bladder was quite closed off by stenosis of the cystic duct, and contained pus but no bile. The bacilli may have grown in the dilated choledochus or in the intestine itself, either after wandering in from the bile tracts or after getting accustomed to the small intestine. The smallest bile tracts in the liver were negative.

He does not think that removal of the gall-bladder in this case would have done the slightest good.

It is interesting to note that he found no typhoid nests microscopically in the bladder wall. He thinks the stones were certainly present before the typhoid attack, though they gave rise to no symptoms. The fresh attack had caused new inflammatory changes and empyema. His conclusion, therefore, was that cholecystectomy can be of no use if the seat of vegetation is in the bile tracts or in diverticula of the upper intestine, and that in no circumstances is the operation justifiable in carriers without positive palpatory evidence before operation.

We have seen that in all the carrier cases mentioned above, which have been operated upon or have come to autopsy, cholelithiasis has been invariably present. The following case, reported by Kamm (1909), which succumbed to pneumonia before the contemplated operative procedures could be undertaken, is of interest as showing that gall-stone formation may be absent in chronic carriers. The patient was a female lunatic (61 years old) who passed through an attack of enteric fever in March, 1906. Typhoid bacilli were present in her stools during the attack and were also demonstrated on the following dates: 9th April, 7th May, 28th May, 2nd June, 11th June, 28th July, 11th September, and 7th November, 1906. Isolation had an unfavourable effect on this woman, who suffered from chronic mania. In 1907 typhoid bacilli were found in the fæces (but not in the urine) on the following occasions, viz., 18th January, 15th March, 10th June and 26th July. The female warder who attended to this patient contracted enteric fever on 18th October, 1907. The operation for removal of the gall-bladder was arranged for 30th October, but had to be deferred owing to the onset of croupous pneumonia. Death took place on 20th November, 1907. At the autopsy, in addition to the pulmonary lesion (croupous pneumonia of right lower lobe) there was marked interacinar cirrhosis of the liver, but the gall-bladder showed no inflammatory changes and contained no stones.

Typhoid bacilli were recovered from various parts of the liver, the gall-bladder, and the duodenum, but not from any other organ. The gall-bladder on microscopic examination showed complete loss of surface epithelium, and in the innermost layers of the mucosa numerous large masses of micro-organisms were found, some of which resembled the typhoid bacillus morphologically and did not retain Gram's stain. It should be mentioned that the post-mortem examination was carried out 28 hours after death, and that organisms of the B. coli type were invariably associated with the B. typhosus. There was no evidence whatever that the typhoid carrier state had contributed to the fatal issue of the croupous pneumonia.

It is unfortunate that Kamm does not mention specifically whether the pneumonic areas in the lung were bacteriologically examined.

The last case to which I shall refer is that of Miss S., one of the female carriers reported by Watt (*vide* page 48). Operation was indicated in this case largely because of the depressed mental attitude of the patient, resulting from a knowledge of the numerous infections she had given rise to in others, and also because of the fact that for many years she had suffered from attacks of indigestion and biliousness. I am indebted to Mr. H. M. W. Gray, Surgeon, Royal Infirmary, Aberdeen, for kindly providing me with notes of the operation, which took place on November 12th, 1908.

The gall-bladder was only with great difficulty exposed owing to dense peritoneal adhesions in its neighbourhood (tuberculous peritonitis). It was of large size, and presented a diverticulum which occupied a recess in the liver. Two large gall-stones were found, from which the B. typhosus was recovered. Unfortunately the patient took the anæsthetic badly, and the contemplated removal of the gall-bladder and its diverticulum had to be given up.

Drainage was therefore resorted to as quickly as possible. Six weeks later the patient died from an aggravation of her lung trouble (phthisis pulmonum). Bacteriological examination of the bile invariably revealed typhoid bacilli. Unfortunately no examination of the fæces was made after the operation, so that it is impossible to say what effect drainage of the gall-bladder had on the excretion of typhoid bacilli. An autopsy could not be obtained.

I conclude this review of the operative treatment of carriers with the reflexion that no trustworthy evidence of permanent cure has so far been forthcoming, As I have indicated in a previous chapter, it may well happen that in cases of cholecystitis occurring at an early period in typhoid convalescence, surgical interference may be followed by a complete disappearance of typhoid bacilli from the fæces, but in long-established cases where the infective germs have acquired a permanent footing not only in the gall-bladder but also in the biliary tracts and duodenal recesses, the prospects of success by operation directed solely to the gall-bladder are extremely small. No definite verdict, however, on the efficiency or otherwise of this method can be pronounced until the cases so treated have been under bacteriological supervision for at least one or two years thereafter.

The treatment of intestinal carriers by typhoid vaccines has, it must be confessed, been unsuccessful or indecisive, though much was hoped from this method. As long ago as 1902 Koch suggested the employment of typhoid vaccines as a remedy for the carrier state. Thomson and Ledingham (loc. cit.) have treated five female carriers in this way with entirely negative results whether stock vaccines or homologous vaccines were employed. In most of the cases where serological examinations have been made, we have noted a marked rise in the agglutinins, but in a recent case treated solely with the homologous vaccine, no appreciable alteration took place in the agglutination-titre. In a recent report by the Director-General of the Army Medical Service (1909) an account is given of the vaccine treatment of an intestinal carrier Private L. both with stock and homologous vaccines, and a temporary cessation in the excretion of the germs in the stools was noted during the course lasting from February–May, 1909. Later, this case received X-ray treatment in the region of the gall-bladder. The carrier presented symptoms of slight cholecystitis, and this form of treatment might, it was hoped, bring about an increase of phagocytosis in the walls of an inflamed gall-bladder.

On 6th August, 1909, the treatment was begun, the gall-bladder region being exposed for three minutes to a 3-ampère current in a tube with a 6½-inch spark-gap. (Report by Cummins 1910.) Exposures were given three times a week for three weeks, and during this time and for three weeks afterwards the stools were typhoid-free. Positive results were, however, got on September 20th, 23rd, and continuously from October 4th to October 21st. Another X-ray course was commenced on October 20th and ended on November 15th. On November 1st the stools were positive, but examinations on November 5th, 9th, and 12th, and December 6th were negative.

The patient left hospital on November 16th. The outcome of this treatment, as perhaps showing some inhibitory action on the discharge of bacilli, is certainly interesting and suggestive, but at present it would be premature to signalize this method as affording a prospect of permanent cure. As a matter of fact the discharge of bacilli by the patient had been intermittent before commencement of the treatment. The method, however, deserves a further trial. The fæces and urine of this man, who is now a civilian, were examined by me on 3rd March, 1910, with negative results, but on June 4th, 1910, I. isolated the B. typhosus from his fæces, so that he cannot be considered as cured.

In another army carrier the method was tried but without the slightest effect on the discharge of typhoid bacilli.

In concluding this chapter we have to deplore the fact that so far the attempts to cure intestinal carriers have not yielded results affording convincing evidence of their success. It must indeed be admitted, on consideration of all the evidence adduced by the surgeon and the pathologist as to the nature of the lesions met with in carriers, that the problem of effecting a cure in these carriers is an extremely difficult one. In the case of carriers who are in an early stage of this condition, there may be some hope of effecting a permanent cure by one or other of the methods already tried and quoted above, but in long standing chronic cases the prospect of success of this kind would seem to be extremely remote.

It may be possible to diminish the number of carriers by some modification of the regime employed in the treatment of enteric cases. This is a question, however, on which I do not feel qualified to hazard any personal opinion, but it may be of interest to note that G. Mayer's (1910) observations led him to believe that an exclusive milk-diet during the disease and an abundance of milk during convalescence were most favourable in diminishing the crop of carriers. With a mixed diet on the other hand, the carrier-state was more likely to intervene. The data on which he founded this opinion (which is supported by Drigalski) were not, however, sufficiently extensive to admit of reliable conclusions being drawn.

I have already sufficiently alluded to the now universally recognised conception of enteric fever as essentially a septicaemic infection and to the animal experiments which show that the gall-bladder invasion occurs at an early stage through the medium of the blood and not by a later inroad from the intestine. Can we diminish or influence in any way the degree of this initial septicaemia? In the absence of an efficient antityphoid serum which would probably have this desired end, one can at present, in the light of certain experimental results obtained by Hilgermann (1909-*b*), only suggest the use of salicylates as a means of arresting or diminishing the typhoidal invasion of the gall-bladder and bile tracts.

The treatment of urinary carriers is discussed in the following chapter.

CHAPTER X.

URINARY CARRIERS.

Pathogenesis of the Condition and Treatment.

In the course of investigations on the carrier problem, urinary carriers have been met with much less frequently than intestinal carriers. The great majority of the chronic carriers discovered in connexion with endemic typhoid fever have been passing the typhoid bacillus in the fæces only and not in the urine. Certainly the typhoid bacillus is occasionally found in the urine of chronic intestinal carriers, especially of the female sex, but in these cases their presence in the urine is almost certainly due to fæcal contamination of the urine. When catheter specimens have been taken (in a few instances recorded) the urine has been invariably free from typhoid bacilli. I may here, however, give the data regarding the occurrence of B. typhosus in the urine of certain chronic intestinal carriers who have been examined over long periods.

1. From June, 1908, to July, 1909, the excreta of Mrs. H. (*see* Thomson and Ledingham (1910)) were periodically examined. The fæces were positive on 29 out of 34 occasions, while the urine was positive on 8 out of 26 occasions. On no occasion was the urine positive while the stools taken at the same time were negative. (*See also* Table at close of Chapter XII.)

2. "G." Female asylum carrier. Period of observation, September, 1907, to February, 1910. Fæces were examined on 41 occasions and were positive on 26. Urine was examined on 33 occasions and was positive on 4, viz., 24th September, 1908,

6th November, 5th December and 11th December. On one of these four occasions the fæces taken at the same time were negative, the explanation probably being that if the number of bacilli discharged is small and the urine happens to get contaminated, their demonstration in the latter is much less difficult. (*See also* Table at close of Chapter XII.)

3. "McC." Female asylum carrier. Period of observation, November, 1907, to February, 1910. Fæces were examined on 38 occasions and were positive on 31. Urine was examined on 29 occasions and was positive on 4 successive occasions, viz., 27th November, 5th December, 11th December, 1908, and 23rd January, 1909. (*See also* Table at close of Chapter XII.)

4. "C." Female asylum carrier. Period of observation, November, 1907, to February, 1910. Fæces were examined on 38 occasions and were positive on 13. (Intermittent carrier.) Urine was examined on 27 occasions and was positive on 1, viz., 5th December, 1908. (*See also* Table at close of Chapter XII.)

Carriers 2, 3 and 4 are isolated in the same building, and the coincidence of the dates on which the urines were positive would seem to suggest that about this period the samples of urine forwarded had become contaminated by fæcal material.

In chronic intestinal carriers of the male sex I have never found the urine positive.

Though in chronic intestinal carriers the occurrence of typhoid bacilli in the urine is rare, it is not so uncommon to find both fæces and urine infective in the acute or transitory carriers and in early convalescent carriers. In this connection reference may be made to the data regarding transitory carriers in Scheller's milk-spread epidemic. Some of these passed typhoid bacilli in the fæces only, some in the urine only, and some in both fæces and urine. In such cases one may suppose that there is a transient typhoidal septicaemia.

The true urinary carrier passes the typhoid bacillus in the urine only, and it is fortunate that such cases are so infrequently met with, as the danger of spreading infection by the urine is much greater than in the case of intestinal carriers.

The earliest cases of this condition were reported about the same time by Rousing (1898), Houston (1899), and Young (1900). It will be advisable to give an account of some of these cases in detail as they tend to throw some light on the pathogenesis of the condition.

Rousing's case was a male of 53 years who had had enteric fever 18 months previously. During the primary attack there had been no retention of urine and no necessity for catheterization. In convalescence the urine was milky and on standing, a heavy deposit formed. Several months later he began to have vesical pain and frequency of micturition especially at night. The urine was acid and contained pus but no blood.

The typhoid bacillus was present in large numbers in the urine. A suprapubic cystotomy was performed and the mucosa was found to have a dark red colour with numerous ulcerations separated by swollen rugae. Cloudy urine came from both ureters. The patient died one month after operation. At the autopsy the right kidney was enlarged and small abscesses were scattered about the kidney substance. The pelvis contained a stone of the size of a walnut and the pelvic mucosa was also swollen and ulcerated. The left kidney was in a similar but less marked condition, with millet seed abscesses in the cortex but no stone. There was no evidence of tubercle. Rousing believed that the calculus had been present for some time before the attack of typhoid fever, and that the trauma caused by it determined the localisation of the B. typhosus in the kidney.

It is known that some cases of nephrotyphoid may be associated with focal abscesses in the kidneys, but they are rare. (*Vide* Flexner (1896).)

Houston's case was a female of 35 years who presented no definite evidence of a primary typhoid infection. Three years before coming under observation she had been living in a house where two children died, one of bronchitis and the other of diarrhœa (patient's diagnosis). She had helped to nurse these children. Shortly afterwards she suffered from frequent micturition which, latterly, was accompanied by pain.

In 1895 (December) she had gone to hospital where she was treated for three months for painful and frequent micturition and occasional passage of blood. She returned to work, but in May, 1898, she again consulted a doctor who, after treating her for cystitis, sent her to hospital where her condition was thoroughly investigated. Her urine was turbid and opalescent, strongly acid and contained a small amount of albumen. The sediment contained numerous squamous cells with pus cells and bacteria. The typhoid bacillus was repeatedly recovered from the urine.

Her serum also agglutinated a known strain of the typhoid bacillus in a dilution of 1 in 100. She remained in hospital for six weeks without showing any abnormal temperature or other symptoms pointing to typhoid fever.

It was from this case that Houston drew the important conclusion that typhoid fever is a true general infection and not merely of local origin in the Peyer's patches of the intestines. This view was elaborated more fully by Horton-Smith (1900) in his Goulstonian lectures of the following year. This author held that the mesenteric glands are the primary seat of the typhoid infection, a view which by several years anticipated that of Forster. (*See also* Levy and Gaehtgens (1908).) With regard to the presence of the typhoid bacillus in the urine of typhoid patients Horton-Smith found positive results in 25 per cent. of cases examined. This is the percentage found in most recent work on the subject of typhoid bacilluria. Of 289 post-mortems in St. Bartholomew's Hospital on typhoid patients (during 30 years) Horton-Smith notes that abscesses of the kidney occurred only once. He believed that the typhoid bacillus grew in the bladder, the walls of which were chronically inflamed.

Young's case (also reported by Gwyn (1899)) was a male of 39 years who had had typhoid fever in 1893. On admission to hospital at that time he had shown pyuria, and one of his complaints was pain during micturition. Ten days after defervescence a relapse occurred but the pyuria continued. In 1897 the urine

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was very purulent and the B. typhosus was first isolated from it in 1898. His serum gave a positive Widal reaction.

In January, 1900, he returned to hospital when the urine was again positive. By cystoscopic examination a chronic ulcerative cystitis was found. There was also a secondary infection with the gonococcus, both gonococci and typhoid bacilli being isolated from the bladder. The fact that this patient also had syphilis in 1889 may have had some influence in predisposing the genito-urinary tract to particular and prolonged infection by the typhoid bacillus.

I have already referred to the cases of Irwin and Houston and Niepratschk, both of which were responsible for fresh cases of typhoid in their vicinity (Chapters III. and VI.).

Greaves (1907) reported the occurrence of a typhoidal pyonephrosis in a patient of 36 years who had had his primary attack of enteric six years previously. From the pain during micturition and the swelling in the left renal region a diagnosis of renal trouble was made and cystoscopic examination revealed that the left kidney was not functionating. At operation, a pyonephrosis was found with a phosphatic calculus in the left ureter. From the pus the typhoid bacillus was recovered in pure culture. Fourteen days after the operation the patient's blood serum agglutinated the typhoid bacillus in a dilution of 1 in 200.

Another important urinary case also associated with pyonephrosis and treated surgically with success was reported by Adrian (1908), and also more fully by Meyer and Ahreiner (1909). The patient was a girl who in 1897 (when six years of age) suffered from pyonephrosis. While under treatment in hospital for this condition she contracted typhoid fever, the pyonephrosis apparently antedating the typhoid attack. Shortly after her discharge home she infected a brother and both her parents with typhoid fever. For 10 years the girl remained perfectly well. Then gradually she began to suffer from acute pains in the left kidney region with swelling of left side of abdomen and thighs, and cloudy urine. A communication had evidently been established between the sac and the bladder, so that the typhoid bacilli vegetating in the sac were continually being discharged by the urine. In July, 1907, nephrectomy was performed. Typhoid bacilli were present in pure culture in the purulent contents of the sac. The actual seat of vegetation had very probably been an ulcerated area which was found near the ureteral orifice. Eight days after the operation bacilli were found in the urine, but afterwards it remained quite free of typhoid bacilli. Before operation the patient had given a Widal reaction of 1 in 10,000, but after operation the titre fell to 1 in 150.

These urinary cases bear a strong analogy to the gall-bladder cases, and therefore one would require to exercise the same caution in judging of the effect of operation. The absence of typhoid bacilli in the urine in the above case after operation certainly suggests that there were no secondary depôts in the bladder itself as one would have expected in such a chronic condition.

Sufficient data have not yet accumulated with regard to the organic lesions associated with the urinary carrier-state to enable us to formulate lines of treatment applicable to particular cases. It would be well, however, whenever opportunity offers, to examine these cases with peculiar care, employing the modern methods of cystoscopy and ureteroscopy, so that the sum total of definite knowledge on this subject may be increased.

That the principal depot of the B. typhosus may be a chronically inflamed or cystic renal pelvis is known, and this may or may not be associated with secondary depots in an inflamed bladder. The latter organ, however, is most probably the main depot in most cases, and the chronic typhoid bacilluria may be regarded as being due to some unwonted vulnerability of the bladder mucosa. The ordinary bacilluria occurring during the fever, may not be associated with any cystitis, but should retention occur, or should the bladder mucosa be more severely damaged than usual by the typhoid toxæmia, a more or less chronic unhealthy state of the mucosa is apt to be set up which may permit the indefinitely prolonged vegetation of the typhoid bacillus. Antecedent inflammatory conditions in the urinary tract may also, doubtless, predispose to the urinary carrier state.

We have not yet sufficient data to enable us to correlate the pathological findings met with in urinary carriers, with those found either in the so-called nephro-typhoid or in cases of acute typhoidal cystitis associated with definite lesions in the bladder. On this latter subject the articles by Schuder (1901) and Schaedel (1906) may be consulted. With regard to the kidney, Cagnetto and Zancan (1907) have shown that in most cases of typhoid fever, inflammatory foci (so-called lymphomata) with focal necroses or even minute abscesses are to be found. These, like the analogous small cell infiltrates described in the liver in fatal cases of typhoid fever, may also act as vegetation-depots of the typhoid bacillus, in the urinary carrier.

Treatment of Urinary Carriers.

Urotropin has proved so valuable in the bacillurias occurring during typhoid fever and in early convalescence from that disease, that one naturally anticipated a similar efficiency in urinary carriers. Such hopes have not been realised so far as the recorded reports show, and, perhaps, the reason of its failure is to be sought in the chronically inflamed and rugose state of the bladder, which may render the typhoid bacillus less readily accessible to its influence. Urotropin certainly has a marked temporary effect in reducing the number of bacilli excreted, but the latter return in full force when the administration of the drug is suspended.

The treatment adopted by Niepratschk (*vide* Chapter VI.) in his case, is so instructive that I give it in detail.

The carrier was isolated on 23rd February, 1908, and treatment with urotropin was at once begun.

First course of urotropin.

23rd February, 1908. Received 1 gm.
24th February–8th March. Received 2 gm. daily.

Result:—Soon after the commencement of the treatment the urine became clear and the number of bacilli decreased. On 26th February, the urine contained only 10,000 bacilli per cub. cent., and

and on 28th February none. On 17th March, when the remedy had been stopped for seven days, the bacilli were as numerous as ever.

Second course.

17th March–24th March. Received 3 gms. daily (=24 gms. in all), and a further 11 gms. up to 6th April.

Urotropin was then laid aside and hetralin—a compound containing 56 per cent. urotropin and 44 per cent. resorcin—was tried.

Hetralin course.

15th April–18th April	2 gms. daily.
19th April–16th May	3 gms. ,,
17th May–24th June	5 gms. ,,
25th June–2nd July	6 gms. ,,
3rd July–11th July	8 gms. ,,

The carrier's health was not affected by the drug. His appetite remained good. A reduction in the number of bacilli resulted, but it was not permanent.

Borovertin, a compound containing urotropin and boric acid (= hexamethylen tetramin triborate) was finally tried with apparent success.

Borovertin course.

23rd July–27th August. 6 gms. daily (= 1 gm. six times a day, and later 1·5 gm. four times a day).

This drug was not so well tolerated as the others. The patient suffered from loss of appetite and weakness, and his body-weight fell from 81 kilo to 70 kilo during the short period from 1st to 29th August. The drug was therefore stopped and the patient recovered very quickly. The disinfectant action on the urine was, however, remarkable. Two days after the first dose, bacilli were still present in considerable quantities, but, thereafter, none could be demonstrated by repeated examinations. Examinations on 27th July, 31st July, 3rd August, and many following days were negative. On 23rd October a litre of the urine was treated by the precipitation method employed in searching for B. typhosus in water, but the result was negative. As large a quantity as two litres was also examined without result.

On 1st November, 1908, Sergeant B. was considered "cured" and resumed his regimental duties. Weekly or bi-weekly examinations of his urine were still continued, but all were negative, and Niepratschk, writing in December, 1909, says that no further cases of typhoid fever have occurred in Sergeant B.'s regiment although he occupies his old position in the barracks.

What impresses one in the recital of this case is rather the systematic and persistent method which was adopted than the ultimate result. If this case may be chronicled as a "cure," it is a remarkable testimony to the efficacy of the drug treatment that a carrier of such long standing, presenting in all likelihood lesions of a chronic character in his urinary tract, should be so completely restored to a normal condition. Any further data regarding the after history of Sergeant B. will be welcomed. In the meantime it may be said that borovertin either alone or perhaps, preferably, after a preliminary course of urotropin, should be given a trial in urinary carriers.

Recently another cure by borovertin has been reported by Ustvedt (1910), but I have been unable to secure full details of the case. The carrier was a ship steward, who continually excreted typhoid bacilli in his urine. After a six weeks' course of borovertin (120 gms. altogether) the bacilli disappeared.

I now come to the treatment adopted by Irwin and Houston (*loc cit.*) in their female carrier case (*vide* p. 38).

For the first five weeks tonics and urinary antiseptics were tried, but with no effect on the bacilluria. Headaches and gastric pain were still complained of. Vaccine treatment was then resorted to, the homologous strain being employed in the preparation of the vaccine.

Course of Vaccine treatment :—

August 25th, 50 millions. Urine positive on September 1st.

September 2nd, 100 millions. Urine positive but bacilli less numerous on September 16th.

September 20th, 200 millions. Urine positive on September 22nd. Bacilli as numerous as ever.

The patient was now put on sodium lactate and the urine made alkaline.

Urine negative on October 8th.

October 9th, 300 millions. Urine negative on October 20th.

October 23rd, 500 millions. Urine negative on October 24th. Clear with no pus and no albumen. Urine and fæces negative on November 21st.

November 21st, 1,000 millions. Urine negative on November 23rd. Fæces negative.

During the treatment, the headaches, gastric pain and feeling of tiredness disappeared, and the patient gained markedly in weight. (The last examination which was negative was made on April 24th, 1909 (Houston (1909)).

The authors believed that by rendering the urine alkaline the typhoid bacilli became more susceptible to the action of the immune bodies developed in the serum by the vaccinations.

Houston (1909) has treated two other urinary cases with typhoid vaccine, but a definite report cannot yet be given.

Two chronic urinary carriers invalided from the Indian army have been treated with typhoid vaccines (Fawcus, Kennedy and Cummins (1910)) in this country, but no definite improvement in their condition was realised. These cases had previously been treated with urotropin without effect, but it was noted that when a diuretic ("sanmetto") was given in combination with the urotropin, a marked fall in the bacilluria took place and the purulent deposit became almost nil. On cessation of the treatment, however, the bacilli were discharged again in large numbers. Major Cummins suggests that more definite results might be attained by combining sanmetto and urotropin with vaccine treatment; but in the light of Niepratschk's results it may be contended that it is the persistent pushing of treatment over a prolonged period that is most likely to be of value in the end.

CHAPTER XI.

DIAGNOSTIC METHODS EMPLOYED IN THE SEARCH FOR CARRIERS.

The demonstration of the typhoid bacillus either in the fæces or in the urine, is essential before a person can definitely be certified to be a carrier.

In dealing with large institutions, however, where enteric fever has been endemic, some indication may be got of the presence of carriers by carrying out an extensive series of Widal tests, commencing with those subjects who are ascertained to have suffered from typhoid fever in previous years or who may happen to present symptoms of gall stone trouble.

It is stated by Kayser (1909) that about 75 per cent. of carriers give a well-marked Widal reaction, but I am inclined to think that this percentage is rather high, if agglutination at 1 in 100 be taken as the criterion of a positive Widal reaction. Of nine chronic carriers whom I have personally observed, five gave a definitely positive reaction, while four gave an incomplete or absolutely negative reaction. On the other hand, in institutions, a positive reaction is occasionally obtained in persons whose fæces, though repeatedly examined, fail to show the presence of the typhoid bacillus. Certainly in such cases, we have to reckon with intermittent periods, imperfect bacteriological methods and possibly other factors not yet fully understood. Kamm (1909) had an experience of the Widal test which was unfortunate and perhaps exceptional. He commenced the search for carriers in an asylum by the examination of 136 blood samples. Four of these gave a reaction of 1 in 50, one gave a reaction of 1 in 100, and three gave a reaction of 1 in 200. Of these eight persons, four had had enteric fever about eight or twelve years previously, while in the other four, there was no record of typhoid. Castor oil was given to these eight persons, and their fæces repeatedly examined thereafter, but in none of them could he demonstrate the typhoid bacillus. It would be interesting to know the further history of these cases and whether definite carriers were ultimately discovered.

Eccard (1910) in the course of his examination of an asylum (*vide* Chapter V.) commenced by performing Widal tests in all departments of the building. The figures obtained he does not record, but he was able to classify the inmates into three groups :—

1. Those who gave no Widal reaction.
2. Those with Widal reaction of 1 in 50.
3. A small number who almost always gave a reaction in 1 in 100. The stools of this group were frequently examined and in five of them he was able to demonstrate the typhoid bacillus. In three others of this group who frequently gave a reaction in 1 in 100, he could never demonstrate typhoid bacilli in the fæces.

An important point noted by him in the course of this investigation was that in a large number of those who were Widal-free or who occasionally gave a reaction in 1 in 50, the titre would suddenly spring to 1 in 100 with symptoms of intestinal disturbance, vomiting and diarrhœa. After the attack the titre again fell.

Some trouble was experienced with three severe tubercular cases who gave positive Widal reactions. One of these died but there were no signs of typhoid fever. (He makes no mention of the condition of the gall bladder) This question of positive Widal reaction in cases of tubercle is discussed in Chapter XII.

Eccard, however, thinks that, at least as a preliminary step, the Widal test should be employed in large institutions, a titre of 1 in 50 to be regarded with caution and one of 1 in 100 as suspicious. He does not appear to have met with carriers who give practically no reaction even in 1 in 20.

When proper bacteriological conveniences are available, the best method of procedure is the immediate examination of the excreta of all persons concerned, commencing with those who give some history of having passed through a typhoid attack or who suffer from gall stones, and then passing on to the others. At the same time Widal tests should be carried out and repeated bacteriological examinations made at intervals, in those cases which give a positive Widal reaction.

It is impossible here to describe in detail the various media employed or recommended for the isolation of the typhoid bacillus from the excreta. For those interested in this subject a list of these media will be found at the end of this chapter.

Amidst a plethora of methods and modifications of methods, all of which are probably excellent in the hands of those accustomed to them, it seems to me of far more importance to obtain a thorough knowledge of the potentialities and the working efficiency of one medium, than to be continually changing from one medium to another without a clear knowledge of the advantages to be derived by the change. Many of the newer media introduced for the isolation of the typhoid bacillus have been recommended strongly on their merits as inhibitors of the B. coli group, but the data on which such judgments are based, have usually been obtained by practice with artificial mixtures of B. typhosus and B. coli, to which the particular medium or inhibiting agent in the medium is added, and not with the actual fæces of typhoid patients or carriers. The writer's experience has been confined to the bile-salt-lactose-agar medium of MacConkey (1901), with neutral red as indicator. This medium has been in constant use for many years and has proved eminently satisfactory. The actual method is briefly as follows :

For Fæces.—About two to three large loopfuls of the fæces are emulsified in broth and allowed to sediment for an hour. From the upper portion of the fluid, two small loopfuls are removed and spread by means of a bent glass rod over two or three Petri plates containing the solidified medium, which should be quite dry. On the following day, colourless colonies suggesting the typhoid bacillus are picked off and inoculated into mannite-peptone-water. If acid only is formed in any tube or tubes and no gas, the probability is strong that the organism is the typhoid bacillus (or the dysentery bacillus—Flexner-type), but it must be remembered that the fæces contain a small group of organisms whose characters in some particulars, present a strong similarity to those of the B. typhosus (Morgan and Ledingham (1909)). As a rule these organisms give little trouble and can be readily differentiated by the application of fermentation and agglutination tests.

The B. typhosus gives an acid reaction without gas formation on glucose, mannite and sorbite ; a late acid reaction on dulcite (Penfold (1910)), (Grattan (1910)) and no reaction on cane sugar or lactose. Indol is tested for by Ehrlich's method (*vide* Marshall (1907)) after four days' growth on broth, and finally an agglutination test is made with a potent antityphoid serum which agglutinates a known strain up to 10,000 or 20,000.

Some workers commence the investigation of a suspicious colony by performing an agglutination test, but it frequently happens that typhoid bacilli taken directly off the plate and tested with an anti-serum, give a very feeble and unconvincing reaction. Scheller (1908) has observed quite a gradation of agglutinability in typhoid colonies taken directly from the same plate. Media containing certain inhibiting agents like malachite green, have been found to reduce the agglutinability of typhoid bacilli when examined directly.

By performing the agglutination test after sub-culture on broth, all the strains which I have isolated from MacConkey plates (either from fæces or urine) have without exception agglutinated up to 1 in 5,000 or 1 in 10,000.

Further, by preliminary performance of the fermentation tests, one acquires a knowledge of the characters of the many members of the non-lactose group whose appearance on plates may simulate strongly that of the typhoid colony, which may indeed give a slight reaction with a potent antityphoid serum, but which can be absolutely excluded by their fermentation and other properties.

A motile non-lactose-fermenting organism producing a permanent acidity on litmus milk and no indol, rendering glucose, mannite, and sorbite, but not cane sugar, acid, has invariably satisfied the agglutination test when finally applied. The rare occurrence of a non-motile or temporarily non-motile typhoid strain has been reported on at least two or three occasions. Those recorded recently by Ernst (1908) and Fischer (1909) ultimately recovered their motility after cultivation on various media. Such a strain I have also encountered on one occasion. It gave all the fermentation tests and the agglutination and absorption tests, but in spite of various methods of culture and animal passage, it has not so far given evidence of motility. The strain referred to was obtained from the stools of a female lunatic in the course of investigations in an asylum. Further samples of fæces were negative, and it seems quite possible that this woman had been a so-called temporary or acute carrier.

It has already been mentioned that frequently the stools of typhoid carriers give practically pure growths of B. typhosus on plates, and there is little trouble, therefore, in isolating them in such circumstances. I have not observed that on these occasions the stools are unusually loose in character, but on the other hand there seems to be no doubt that after a period of constipation it may be possible to encourage the appearance of the bacillus in the fæces by the administration of a mild purgative or cholagogue.

The isolation of B. typhosus from the urine in urinary carriers, is, as a rule, very easy, as it is generally the only organism present. Some difficulty is said to have been encountered in getting organisms isolated from urine to agglutinate properly, but this has not been my experience.

The diagnosis of carrier cases by serological methods (opsonins or tropins, or complement-deviating bodies) can only be regarded as adjuvants to the ordinary bacteriological routine. This subject will be discussed in Chapter XIV. (*see also* Hamilton, 1910).

Finally, I may refer to an interesting, though not very practical, method of demonstrating the presence of B. typhosus in a carrier who may not at the time be actively shedding the bacillus in the fæces. Weber (1908) passed a dose of oil (about 200 c.c.) into the stomach, thereby causing a regurgitation of typhoid-containing bile into that organ. After half-an-hour the stomach was emptied and a fluid obtained which presented an upper oily layer and a lower watery bile-stained layer. In two chronic carriers whose stools contained only a very few typhoid bacilli, he was able to recover the typhoid bacillus from the upper oily layer. It is not always possible, however, to obtain this back flow of bile into the stomach.

Media employed for the Isolation of B. Typhosus from the Excreta.

It would take too much space to discuss the respective merits of the many media employed for this purpose, but some reference will be made to the results recorded by those who have had personal experience of their use, or who have instituted comparative tests as to their efficiency. For the preparation of the various media the reader is referred to the original papers (*see* Bibliography).

Only those media which are in current use at the present time will be referred to.

1. Bile-salt-lactose-neutral-red-agar.

MacConkey's (1901) original media did not contain the neutral-red. The latter was added on the suggestion of Grünbaum and Hume (1902).

For full information regarding the development of bile-salt media, the reader is referred to a recent communication by MacConkey (1908), in which the exact mode of preparation is described.

2. Medium of Drigalski and Conradi (1902). Lactose-litmus-nutrose-kristalviolett-agar.

The preparation of this well known medium is described in most bacteriological text-books. On the Continent its use is now very largely superseded by media of more recent development. (*See* below).

3. Medium of Endo (1903). Lactose-fuchsin-sodium-sulphite-agar.

4 Method of preliminary enrichment by caffeine. Roth (1903), Ficker and Hoffmann (1904), Lubenau (1907), Werbitzki (1909).

The fæcal material is incubated in the caffeine enriching solution and finally plated on Drigalski-Conradi plates.

Caffeine has also been added with advantage to fuchsin media (Gaehtgens, 1905), and malachite-green media (*see* below).

5. Media containing malachite-green, introduced by Loeffler (1903) and since modified and improved by himself and others.

(*a.*) Malachite-green-nutrose-agar. Loeffler (1906).
(*b.*) Malachite-green-bile-agar. Loeffler (1907).
(*c.*) Malachite-green sodium sulphite-bile-agar. Padlewski (1908).
(*d.*) Malachite-green-safranin-reinblau media. Loeffler, Walter, Dibbelt, and Wehrlin (1909).
(*e.*) Method of Lentz and Tietz (1903, 1905) in which the malachite-green medium is used mainly as an enriching medium, the growth being subsequently plated on Drigalski-Conradi or Endo plates.

(This is the method in current use at the Strassburg Institute) (*see* below).

6. Brilliant-green-picric-acid-agar. Medium of Conradi (1908).

Fawcus (1909) has modified this medium by adding to it bile-salt and lactose.

7. China-green-agar. Medium of Werbitzki (1909).

During the last two years some important comparative trials have been made of these various media, but, as might have been expected, the results have shown little unanimity. It would appear, indeed, that the media which prove most efficient in these trials are those with which the various authors themselves have had most practical experience. The results certainly bear out the statement made earlier in this chapter that a thorough knowledge of the capabilities of these media under all conditions is essential before one can arrange them in an "efficiency-scale." It may be of interest, however, to cite some of these results as they may prove of value to workers in this field.

Schumacher (1909*b*) has compared the efficiency of the recently-introduced Conradi medium (brilliant-green-picric acid) with that of Endo, employed either alone, or after enrichment on malachite-green.

The latter was the method then in constant use at the Institute in Trier.

500 samples of excreta (suspected to contain B. typhosus) were plated on these two media simultaneously, the amount of material plated being the same in each case.

Results :—

Endo plate alone ...	45 positive results	= 9 per cent.
Endo plate + malachite-green enrichment ...	50 „ „	=10 „
Brilliant-green picric acid (Conradi) ...	54 „ „	=10·8 „

So far as the percentages go, the differences do not appear very great, but the author on reviewing his results came to the conclusion that the brilliant-green plate materially increased the chances of obtaining positive results. However, in view of the fact that brilliant-green sometimes failed where Endo or malachite-green succeeded, he advised the following combination of the two methods. The material is spread on a brilliant-green plate, then with the same bent rod on a malachite plate, and from this again on an Endo plate.

The majority of the positive results would be got on the Endo or brilliant-green plate, and this may be still further raised by washing off the growth on the malachite plate and replating. This three-plate system is at present in use at Trier, and experiments are being made with the object of combining malachite-green and brilliant-green in one plate.

Kathe and Blasius (1909), of the Hygiene Institute in Halle, have reported on a series of comparative tests made with the following media :—

Malachite-green-Drigalski (Lentz-Tietz).
Endo.
Brilliant-green-picric acid (Conradi).
Malachite-green-bile-agar (Padlewski).

The material employed was the fæces and urine of patients, in whom a definite diagnosis of enteric fever had been made, either by successful isolation of bacilli from the blood, or by the Widal reaction. Samples were taken at various stages of the disease, and both freshly passed material and material several days old was employed. Of each medium, one large or three small plates were spread, with approximately the same quantity of material. The plates were examined after 18–22 hours at 37° C. and again after a further period of 20–24 hours. Attention was paid only to the presence or absence of typhoid colonies and not to their relative numbers. 53 samples in all were examined, viz., 22 of urine and 31 of fæces. With the latter they obtained the following results :—

Malachite-green-Drigalski (Lentz-Tietz)	3	positive results	= 10	per cent.
Drigalski-Conradi	6	„ „	= 19	„
Endo	8	„ „	= 26	„
Brilliant-green-picric (Conradi)	9	„ „	= 29	„
Malachite-bile (Padlewski) ...	10	„ „	= 32	„

On the whole, therefore, the media of Padlewski, Conradi and Endo proved most satisfactory, whereas the method of Lentz-Tietz proved least successful in this particular trial although the authors had carried out exactly the directions recommended by its originators.

As so many others have found, Kathe and Blasius were unable to satisfy themselves of the favouring action of malachite green on the typhoid bacillus and its inhibitory action on B. coli. In their view, the main cause of the discrepancy in the results with malachite green, is to be found in the varying resistance offered by typhoid strains to this agent, some being able to grow on it readily while others are completely inhibited.

There is no one "medium of selection" for the isolation of B. typhosus from fæces. Each medium has its advantages and disadvantages and in order to obtain the maximum efficiency Kathe and Blasius recommend, as Schumacher does, a combination of three media, viz., Padlewski, Endo and Conradi (brilliant green picric acid) with subsequent plating on Endo.

The method they adopt is the following:—Two or three loops are spread on a Conradi plate (brilliant green) and with the same rod, a Padlewski plate is spread.

Two to three loops are also spread on a malachite-green plate and with the same rod an Endo plate is spread. The plates are incubated for 18–20 hours, and if no suspicious colonies are present the Conradi and the malachite-green plates are washed off and plated again on Endo. They are then left for another period of 18–20 hours.

(For information regarding the cost of these media, this paper by Kathe and Blasius should be consulted.)

Other observers, Grimm (1909), Fischer (1909), &c., have reported very favourably on the method of Lentz-Tietz. Thus the former obtained the following results with 25 samples of fæces from typhoid patients or carriers:—

Drigalski-Conradi	9	positive	cases	= 36	per cent.
Malachite-bile-agar (Loeffler)	9	„	„	= 36	„
Padlewski	12	„	„	= 48	„
Brilliant-green (Conradi)	14	„	„	= 56	„
Lentz-Tietz	15	„	„	= 60	„

Fischer's material was 100 samples of fæces which certainly contained typhoid bacilli.

With the methods of Lentz-Tietz, Endo and Conradi (brilliant green) he obtained positive results in 76 per cent., 63 per cent. and 48 per cent. respectively.

Megele (1909), on the other hand, working with the fæces of carriers found Padlewski's method the most efficient. His figures were:—

Drigalski-Conradi	70	per cent.	positive	results.
Conradi (Brilliant-green)	66·6	„	„	„
Malachite-green (Loeffler)	33·3	„	„	„
Padlewski	79	„	„	„

The most recent comparative tests have been made by Gaehtgens and Brückner (1910) of the Strassburg Institute, where the method of Lentz-Tietz is in constant use for the isolation of typhoid bacilli from excreta.

One hundred samples of fæces were examined, viz., 22 from carriers, 72 from typhoid patients, and six from paratyphoid patients during the febrile period. They were plated simultaneously on seven different media with the following results:—

Lentz-Tietz	66	positive	= 66	per cent.
Conradi (Brilliant green) with subsequent washing off	59	„	= 59	„
Caffein-Fuchsin-Agar (Gaehtgens)	58	„	= 58	„
China-green-Agar (Werbitski)	53	„	= 53	„
Fuchsin-Agar (Endo)	50	„	= 50	„
Malachite-green-sodium sulphite-bile-agar (Padlewski)	48	„	= 48	„
Conradi (brilliant green) without subsequent washing off	41	„	= 41	„

The non-success, which Kathe and Blasius had with the method of Lentz-Tietz, they attributed to the fact that the plates had not been incubated long enough. According to Gaehtgens and Brückner the "enrichment" plates should be incubated for at least 24 hours and if only slight growth occurs, for another period of 24 hours. Kathe and Blasius had also used a neutral agar, whereas Gaehtgens and Brückner employed one with a reaction of 1 per cent. normal soda below the Phenolphthalein neutral point. (Modification by Klinger, 1904.) It is certainly significant that the medium with which Gaehtgens and Brückner had had constant experience for five years in the Strassburg Institute should have stood this comparative test so well.

CHAPTER XII.

DISCUSSION OF THE GENERAL QUESTION OF CARRIER-INFECTIVITY.

This question involves the consideration of many factors which must play a part in the successful infection of a new host by a carrier. In the first place, the bacillus has to be transferred directly or indirectly from the carrier to the new host. The degree of likelihood of this transference taking place will depend, perhaps largely, on the personal hygiene of the carrier and the measures of disinfection adopted by him, provided he is cognisant of his condition, and on the method of disposal of his stools and urine. Where the carrier is unaware of his condition, the chances of successful transference are much greater in spite of average personal hygiene, and they are also very much intensified in the case of lunatics of unclean habits. Further, much will depend on the environment and personal hygiene of the new host in so far as these conditions affect his liability to exposure to infection. If these conditions are satisfied, *i.e.*, given carriers and associates of uncleanly personal habits, the probability of successful transference to a new host is greatly enhanced, provided the carrier is actively excreting the typhoid bacillus. Throughout this memoir numerous instances of prolonged intermission (up to two years in some cases) are referred to. Certainly, some of these may be only apparent intermissions, *i.e.*, the bacilli discharged may be so few that our bacteriological methods cannot reveal them. There can be no question that many of the instances of intermittent infectivity cited throughout the earlier chapter of this memoir, are to be explained by the variation in the numbers of bacilli excreted by the carrier from time to time. Obviously the more numerous the bacilli excreted are, the greater is the chance of their being successfully transferred to a new host.

The magnitude of the dose received by the new host is probably a most important factor in determining whether a subsequent infection takes place or not.

Given a successful transference to the new host, there remain for successful infection at least two further factors, viz., virulence of the strain and the individual susceptibility of the new host. With regard to the first, a general notion has prevailed that carrier strains are less virulent than those from acute typhoid cases. As to this there is no sufficient evidence. If, as some authors have done, we take the mortality among the affected as the criterion of virulence, we find entirely discordant conclusions. If, on the other hand, the effect of the bacillus typhosus on animals be selected as an index of its virulence, the evidence hitherto available on this point is found to be inconclusive. As a matter of fact, seeing that the experimental reproduction of enteric fever in animals is impossible, we possess really no reasonably certain experimental criterion of virulence. Intraperitoneal inoculation of the guinea-pig has, however, been widely employed in testing the virulence of typhoid strains, and the variations in the magnitude of the minimal lethal dose for that animal have been shown to bear some relation to the ease with which the bacillus is acted upon by the various antibodies in normal and immune serum (lysins and opsonins).

So far as carrier strains have hitherto been compared with those isolated from typhoid cases in respect to their virulence for the guinea-pig, no marked divergence has been found. The same variations in virulence are met with among carrier strains as among those from acute cases.

Lentz (1905) sent 20 carrier strains to the Institut für Infektionskrankheiten to be tested for virulence, with the result that neither a greater nor a less degree of virulence than that of ordinary typhoid strains could be detected. It cannot be said, however, that enough strains have yet been examined in this respect to justify definite decision on the matter. Most authors have omitted to test the strains they have isolated on the guinea-pig. It is highly important that in performing such tests, as small an interval as possible should elapse between isolation of the strain and the determination of its virulence. I have adopted the following technique in testing the virulence of carrier strains for the guinea-pig.

The fæces are plated in the usual way, and on the following day, if typhoid-like colonies are present, one is touched with the point of a straight needle and inoculated into a fixed quantity of broth (6 c.c.), which is then incubated for 48 hours. A control mannite tube from the same colony is also inoculated, so as to make certain that the colony is really a typhoid colony. Growth for 48 hours in this way gives a fairly constant number of bacteria per cubic centimetre (700 to 800 millions). Guinea-pigs of 250 gram. weight are then inoculated intraperitoneally with falling quantities of the broth culture. The result has been that most of the strains tested kill in 1 c.c., a few in 0·1 c.c., and a few in 2 c.c. There is therefore no evidence of lack of virulence.

Far more important than the isolated virulence test is the periodical test, as there is certainly the possibility that the virulence of the strain may vary at different times of the year in the same carrier. My observations on this point are not on a sufficiently large scale to permit of trustworthy conclusions being drawn, but some results already obtained suggest that some such variation in virulence occurs. For example, a strain isolated from an intestinal carrier on 23rd October, 1909, killed in one-tenth c.c. A culture isolated on 19th November killed only in 1 c.c. On 1st February, 1910, the culture isolated did not cause death in 1 c.c. On 14th February it did not kill in 2 c.c.

However, without much further investigation it would be unjustifiable to assume that the virulence of a carrier strain is much reduced during the winter months. Whether the guinea-pig's susceptibility to the B. typhosus varies in the opposite direction according to the season must be left undecided.

That an avirulent bacillus might suddenly regain its virulence was suggested also by Scheller (1909), who, however, gave no evidence in support of this point.

Niepratsck (1909) who made a very careful examination of the strain isolated from the urine of a urinary carrier (*see* Chapter VI.), found that its virulence for the guinea-pig was distinctly low. By passage through the guinea-pig he succeeded in raising the virulence considerably, and he suggested that a similar increase of virulence might be attained by passage through the human body, and in this way, slight or unrecognised infections might be followed by infections of average severity.

I now come to the second factor involved in the successful infection of a new host by a carrier, viz., the susceptibility of the host. Unfortunately we have no satisfactory method of experimentally estimating the strength of this factor, and our conception of its importance must depend for some time on actual observed facts. Thus we have seen that the typhoid bacillus may be taken into the intestine, may even gain entrance to the general circulation and be passed in the urine without giving rise to any obvious infection at the time. Scheller's (1908) cases in the milk-spread epidemic already quoted (*vide* Chapter IV.), afford one of the most convincing instances of this phenomenon. In view, however, of the demonstration of typhoid bacilli in the fæces and blood during the incubation stage of typhoid fever by Mayer, Conradi and others, it might be expected that some of these so-called temporary carriers would ultimately present symptoms of infection, and Mayer (1910) has actually observed such cases.

It seems appropriate here to refer to certain observations of Busse (1908) on the occurrence of typhoid bacilli in the blood of patients at whose autopsy tubercular lesions only were found.

The first case was a female of 48 years who was suspected to be suffering from typhoid fever. She was admitted to hospital on 31st January, 1907. The typhoid bacillus was twice isolated from the blood, viz., on 1st February and 6th February, 1907, but the serum gave a negative Widal reaction. Death took place on 7th February, 1907. Post-mortem, most of the organs showed miliary tubercules, the lymph glands were caseous, but no lesions pointing to a typhoid infection were detected (Peyer's patches not swollen). The organs, however, were not examined bacteriologically, and no mention is made of the condition of the gall-bladder. Further, what appears to me a point of importance, was the fact that rose-spots were present on the fourth day of her sojourn in hospital. There was no evidence of her having had a previous attack of enteric fever. The second case was also a female of 25 years suspected to be suffering from typhoid fever, who was admitted to hospital on 9th April, 1907. The Widal reaction was negative, but the typhoid bacillus was isolated from the blood on 10th April, 1907. The spleen was palpable under the ribs and apparently also tender. Death took place on the 16th April, 1907. At the autopsy generalised tuberculous lesions were present in the lungs, intestine, peritoneum, &c. There was no swelling of the Peyer's patches, but three ulcers with tuberculous areas at their bases were present in the small intestine. The spleen, lungs, liver, bile and mesenteric glands were bacteriologically examined with negative results. A typhoid-like bacillus was, however, isolated from the bile, but it was not thoroughly examined, which is unfortunate.

In Busse's view, the typhoid bacillus was living a saprophytic existence in these two cases, as in those carriers who have never had any clinical symptoms of a typhoid infection. The blood invasion, he believed, was brought about by an increased permeability of the intestinal wall owing to the tuberculous lesions therein. A phthisical female patient in whom there was no suspicion of typhoid fever was also examined. From her blood the typhoid bacillus was isolated on several occasions although the Widal reaction proved negative. The urine and fæces of this case were examined bacteriologically with negative results.

Further, from the blood of a case of pneumonia the typhoid bacillus was isolated although the urine and fæces were negative. This patient presented symptoms of diarrhœa at first, but the course of the illness proceeded as a typical pneumonia of the right lower lobe. No evidence is afforded, however, proving that the lung infection was not of a typhoidal nature.

Busse's conclusion was that all these cases were probably carriers although they presented no history of having had typhoid fever. The typhoid bacillus, leading a saprophytic existence in the intestine, reached the blood stream as a result of an increased permeability of the intestinal muscosa due to the tubercular lesions. Further, he concluded that the presence of typhoid bacilli in the blood is not an absolute sign of the presence of a typhoid infection.

These results of Busse have to be considered in the light of accumulated knowledge regarding atypical and apparently symptomless enteric fever on the one hand and typhoid carriers with no typhoid history on the other hand. The explanation given by Busse that these cases were really typhoid-carriers, and that a passive invasion of the blood-stream took place as the result of the intestinal lesions, may be a perfectly sound one, but there is nothing in the evidence which entirely excludes the possibility of these cases being really mixed infections of tubercle and typhoid.

In chronic carriers the blood has very seldom been examined bacteriologically, but in the few examinations made, it has invariably been negative. During an exacerbation of cholecystitis, however, the blood may be found to contain the bacilli.

Some years before Busse's observations on this question appeared, Jurgens (1907) had reported the finding of typhoid bacilli in the fæces of a tuberculous patient in the course of an epidemic of typhoid fever. A diagnosis of enteric fever was made, but from the further course of the disease there was no doubt that the symptoms were attributable entirely to the tubercular infection. V. Krehl (1906) also recorded the discovery of typhoid bacilli in the blood of a case which proved at autopsy to be one of miliary tuberculosis. All such cases demand a more thorough bacteriological investigation than has hitherto been accorded them, and it would be advisable in cases of suspected miliary tuberculosis in children to examine whether the blood serum gives a Widal reaction and whether the typhoid bacilli can be isolated from the blood. The literature contains not a few references to the presence of agglutinins for the typhoid bacillus in the serum of tuberculous patients (Jurgens (1907), Krencker (1909) and others) but the most recent observations of Roth (1910) on this subject go to show that such occurrences must be very rare. The latter observer examined the sera of 100 cases of severe pulmonary tuberculosis, including five cases of the miliary form. The dilutions he employed were 1 in 50, 1 in 75, 1 in 100, and 1 in 200. Of this large series, five only gave a reaction in 1 in 50 and one in 1 in 200. This latter case was a man of 44 years who had never suffered from typhoid fever. Five years previously he had had an illness diagnosed as "Influenza." What most of his predecessors in this field had neglected to do, Roth did; he made repeated examinations of this person's fæces, but so far he has been unable to isolate typhoid bacilli therefrom.

Several authors have reported instances which suggest that certain factors such as trauma, pregnancy, the puerperal state, &c. may predispose to infection. Thus Levy and Wieber (1907) report the case of a woman who had her first child on 1st October, 1906. and 12 days later had recovered from the effects of confinement. On 21st October she fell ill with typhoid fever, and the bacillus was found in her fæces. The mode of infection was doubtful, but it was found that her mother had stayed with her in the house since the birth. The mother, who was quite healthy, belonged to a village in which enteric cases had been notified in 1906. During the summer she had had an influenzal attack, which was now judged to be typhoid fever. Her stools were therefore examined and she was found to be a carrier. Thus the woman was apparently infected by her mother, and in Levy and Wieber's view, childbed was the predisposing cause.

Cases of enteric fever in the puerperium have not infrequently been diagnosed as puerperal fever. Levy and Wieber report in illustration of this point, that two epidemics occurred in two villages near Strassburg, the one with 14 cases and the other with 11 cases. They were both ascribed to contact with a typhoid-sick woman in the puerperium whose illness had not been diagnosed as such, but as puerperal fever. Recently I had an opportunity of examining the blood of the umbilical cord, at the confinement of a typhoid carrier who had been under observation for over a year. The typhoid bacillus was recovered from the blood, but organisms of the Coli group were also present so that some fæcal contamination of the blood, while the sample was being taken, could not definitely be excluded. The examination was undertaken in order to determine whether the general disturbance incidental to pregnancy and childbed might induce a general typhæmia. Unfortunately, for the reasons above mentioned, the matter remains not proven. As it was, the child remained quite healthy and the mother made a normal recovery.

Another factor has been insisted on by Conradi, viz., that strangers are most ready to contract infection when they come for the first time in contact with carriers. This proposition is a fascinating one and certain facts observed in connection with outbreaks due to carriers may be regarded as lending it some support.

For example, we have noted that the victims of the New York cook (reported by Soper, *vide* Chapter III.) were frequently new servants who had only quite recently come in contact with her, while the members of the household, who had been served by her for a considerable time, escaped infection. It would be quite legitimate to suppose that the latter had gradually acquired a certain degree of immunity by the ingestion of repeated small doses of typhoid bacilli, while the new servants not so protected would more readily react to infection. There is, however, the further possibility that, owing to the closer contact of the servants with the carrier, the less strict cleanliness in force in the servants' hall at mealtimes and otherwise, and the use of the same privy, the dose of bacilli ingested by the servants would be liable to be greater during any given period than that ingested by the other members of the household.

Davies and Walker Hall (1908) have put forward the view that it is only at certain seasons that carriers are effective and that for every carrier there is a particular season when infection from him or her is most likely to occur. The evidence on which this view is based is not convincing. That carriers generally are more likely to give rise to infection during the summer and autumn months has been frequently commented on and is exactly what might be expected, in view of the greater chances that the typhoid bacillus has, during this period, of prolonging its extra-corporeal existence and multiplying itself before gaining entrance to a fresh host. Intermittency in the excretion of the bacillus by a carrier is certainly not always confined to the same season of the year and may indeed not be observed at all even when the carrier's excreta are frequently examined over a long period. Thus in the Brentry case, Davies and Walker Hall found that the fæces of Mrs. H. were negative during January, February and March of 1908 (three examinations). Further examinations of the fæces and urine of this carrier were carried out by me during the period June, 1908–July, 1909 (Thomson and Ledingham (1910)), and the results are recorded in the annexed table with similar data regarding other carriers who have been under bacteriological supervision for considerable periods.

TABLE showing results of examinations of fæces of chronic carriers (Urine results not shown).

—	Mrs. H.		" G."		" McC."		" C."		" W."		" Ca."		" P."	
	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
1907.														
Sept. ...	—	—	1	—	—	—	—	—	—	—	—	—	—	—
Oct. ...	—	—	1	1	—	—	—	—	—	—	—	—	—	—
Nov. ...	—	2	1	—	2	—	1	—	—	—	—	—	—	—
Dec. ...	1	—	?	—	?	—	?	—	—	—	—	—	—	—
1908.														
Jan. ...	—	1	1	—	1	—	—	1	—	—	—	—	—	—
Feb. ...	—	2	?	—	?	—	?	—	—	—	—	—	—	—
Mar. ...	—	—	—	1	1	—	1	—	—	—	—	—	—	—
April ...	1	—	?	—	?	—	?	—	—	—	—	—	—	—
May ...	?	—	?	—	?	—	?	—	—	—	—	—	—	—
June ...	5	—	—	1	1	—	1	—	—	—	—	—	—	—
July ...	4	—	?	—	?	—	?	—	—	—	—	—	—	—
Aug. ...	2	—	1	—	1	1	—	3	—	—	—	—	—	—
Sept. ...	4	—	1	3	—	1	—	1	—	—	—	—	—	—
Oct. ...	3	—	2	3	3	2	—	5	1	—	1	—	—	—
Nov. ...	2	1	2	1	3	—	1	2	?	—	?	—	3	1
Dec. ...	1	1	2	—	2	—	1	1	1	—	1	—	?	—
1909.														
Jan. ...	1	1	1	—	1	—	1	—	1	—	—	1	?	—
Feb. ...	2	1	2	1	1	2	1	2	?	—	?	—	2	—
Mar. ...	1	—	1	3	4	—	1	3	1	—	—	1	1	1
April ...	2	—	3	—	3	—	1	2	1	—	—	1	—	2
May ...	?	—	2	—	2	—	1	1	1	1	—	2	4	—
June ...	?	—	?	—	?	—	?	—	?	—	?	—	2	—
July ...	3	—	?	—	?	—	?	—	2	—	—	2	1	—
Aug. ...	—	—	?	—	?	—	?	—	1	—	—	1	?	—
Sept. ...	—	—	1	1	1	1	—	2	?	—	?	—	?	—
Oct. ...	—	—	1	—	1	—	—	1	?	—	?	—	2	—
Nov. ...	—	—	1	—	2	—	1	1	?	—	?	—	1	—
Dec. ...	—	—	?	—	?	—	?	—	?	—	?	—	?	—
1910.														
Jan. ...	—	—	1	—	1	—	1	—	—	?	1	—	—	?
Feb. ...	—	—	3	—	3	—	2	1	1	—	—	1	1	—
Mar. ...	—	—	?	—	?	—	?	—	1	1	1	1	1	—
April ...	—	—	1	—	1	—	—	1	—	—	?	—	—	—
May ...	—	—	2	—	2	—	—	2	—	—	1	—	—	—
June ...	—	—	—	1	1	—	—	1	—	—	—	—	—	—
Totals ...	32+	9−	31+	16−	37+	7−	14+	30−	11+	2−	5+	10−	18+	4−

? denotes that no examination was made.

It will be seen that the fæces of Mrs. H. (Brentry carrier) were positive on four occasions out of six, during January, February and March, 1909. G., McC., and C. are the three asylum carriers mentioned in Chapter V., pp. 58–60 (A. and J. C. G. Ledingham). Ca. is the intermittent carrier referred to in Chapter X., pp. 84–85. P. is the chronic carrier who suffers from periodical attacks of gall stone colic., Chapter VII., pp. 73–75.

The carriers C. and Ca. are the only two, in whom the negative results exceed the positive.

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CHAPTER XIII.

STATISTICAL DATA REGARDING THE INFECTIVITY OF CARRIERS.

This important question will receive more adequate treatment as years go on and data accumulate, and when it has become the established practice for the hygienist to co-operate with the bacteriologist in all enquiries into the origin and spread of enteric fever. Hitherto the available data have concerned only individual instances of infectivity, and, except by a few writers, no attempt has been made to employ these data for statistical purposes. Where, however, bacteriological and epidemiological enquiries have run concurrently over a fairly prolonged period, as in south-west Germany, some exceedingly striking facts have been deduced, which point to the not inconsiderable part played by carriers in the spread of enteric fever. I shall consider in the first place the recent report by Kayser (1909) on the incidence of typhoid fever in the town of Strassburg during the period summer, 1903, to spring, 1907 (nearly four years).

There were 505 cases in all (nearly 141 per annum), with a morbidity of 0·92 per 1,000 of the civil population. (In 1905 the population of Strassburg, excluding the military, was 152,271.) 6·3 per cent. of the cases were due to B. paratyphosus "A" or "B" (1 per cent. "A" and 5·3 per cent. "B").

96·7 per cent. of all the cases were examined bacteriologically, and in 87 per cent. the source of infection is said to have been traced with greater or less definiteness.

Thus—

13 per cent. of the cases came to the town already ill.

26·7 per cent. of the cases are stated to have contracted enteric fever by drinking raw milk, either from houses in which there were typhoid patients, or from dairies in which carriers were employed.

14·6 per cent. were attributed to infection conveyed by water (use of spring or canal water), swallowing of infected water in public baths and at water sports, unclean ice, &c.

2 per cent. were attributed to food-poisoning (Paratyphosus "B.")

11·9 per cent. were attributed to infection derived from contact with typhoid fever patients. Almost all these patients had been atypical or undiagnosed cases.

4·9 per cent. were professional nurses in charge of typhoid cases.

2·2 per cent. were washerwomen in contact with typhoid patients.

9·5 per cent. were attributed to infection derived from carriers (= 48 cases).

Kayser notes that some of these cases due to carrier infection were very severe. He considers that the percentage of cases attributed to infection by carriers is probably too low, and states that his figures include only those cases in which the evidence of carrier infection was absolutely conclusive. From an analysis of his cases he concluded that typhoid fever might be regarded as a disease affecting almost exclusively members of certain trades, particularly those engaged in the preparation of food stuffs, cooks, servants, milk-sellers, and bakers. There was also some special incidence on midwives, apothecaries, and hotel staffs.

During the period indicated, 28 carriers were discovered in the town of Strassburg. Of these nine were chronic carriers, eight excreted the bacilli for some weeks or months, while in the remaining persons, including four children, the bacilli were found only once or twice.

Children were never found to be chronic carriers.

Of the 28 carriers, 11 gave rise to typhoid cases in their neighbourhood, nine probably caused other infections, and eight gave no reason for suspicion.

To summarize, carriers accounted for at least 9·5 per cent. of the total cases of typhoid fever during the period under review.

In the cases due to milk, Kayser includes those in which the milk had been infected by typhoid carriers as well as in other ways, so that the total percentage of cases due to carrier infection (direct or indirect) is probably very much higher than 9·5.

Forster (1908) had already reported the figures relative to the typhoid cases enquired into at his institute in Strassburg during the period January, 1906, to end of June, 1907. In that time 386 cases of enteric were investigated, and 77 of these (or 20 per cent.) were attributed by him to carrier infection.

The following table shows, as regards the total number of cases of typhoid fever, the proportions in which infection was attributed to carriers and to contact with persons suffering from the fever respectively.

—	Total cases of Typhoid Fever.	Infection by Carriers.	Percentage.	Infection by contact with the Sick.	Percentage.
1st Quarter, 1906 ...	37	8	22	3	8
2nd Quarter, 1906 ...	62	18	29	27	44
3rd Quarter, 1906 ...	164	17	10	58	55
4th Quarter, 1906 ...	57	17	30	9	16
1st Quarter, 1907 ...	31	8	26	7	23
2nd Quarter, 1907 ...	35	9	26	13	37
Total	386	77	—	117	—

The percentage of cases due to carriers rose as high as 30 in one quarter, and the average for the 18 months under review worked out at 20.

In Forster's view this percentage is probably too low, as it is possible that many of the small water- or milk-spread infections may have been directly due to some carrier-focus acting only for a very short period.

I come now to consider the statistics for the whole campaign during the four years ending 31st December, 1907. The figures for 1904, 1905 and 1906 are given by Frosch (1907). During that time, as I have already observed, there were 6,708 typhoid fever cases of whom 310 became carriers (144 transitory, 166 chronic). Of these 6,708 infections, 215 were in all probability attributable to carriers, and 61 were attributable to carriers with less probability, *i.e.*, 276 infections or 4·11 per cent. of the total number were ascribed to carriers. The figures for the year 1906 are, however, the only ones available for determining the relative shares of carrier and other agencies in the propagation of typhoid fever.

In 1906 there were 2,080 cases of enteric fever, and in 978 the source was explained (*i.e.*, 47·7 per cent.). Of these 978 cases, 642 were attributed to contact with infectious persons (=28·5 per cent. of the total cases, or 65·14 per cent. of the explained cases). Included in the explained cases are 104 in which it was an open question whether direct or indirect contact was involved. Adding these 104 to the cases definitely attributed to contact we get a total of 746 (= 36·02 per cent. of the total cases, or 76·2 per cent. of the explained cases).

232 infections were attributed to drinking contaminated water, contaminated milk, food-stuffs, &c. (= 11·15 per cent. of total or 23·7 per cent. of explained cases).

1·76 per cent. of the total were imported cases.

Of the 642 contact cases, 49 were due to contact with carriers, = 2·35 per cent. of total cases, or 5·01 per cent. of the explained cases.

Thus about one-fourteenth of all contact infections were due to carriers, while the remaining thirteen-fourteenths were due to ordinary cases of typhoid fever.

Before they were discovered 310 carriers caused 228 infections, = 3·41 per cent. of all cases, while after their discovery and the enforcement of requisite precautions, only 48 infections arose from them, *i.e.*, known carriers were responsible for 0·7 per cent. of all infections.

Klinger (1909) in a more recent report gives the figures up to the end of 1907. The carriers had now mounted to 431 and the total number of infections attributed to them was 351, viz., 51 due to transitory carriers and 300 due to chronic carriers.

These numbers appear small in comparison with the total number of typhoid cases, and, if cursorily considered, might be held to imply that the danger from carrier infection was a relatively small one, but it has to be remembered that though a carrier may infect directly or indirectly one single person, the latter may propagate the infection widely. In fact, endemic prevalences of typhoid fever on a fairly large scale have in the last resort been found to be traceable to a carrier who was responsible only for the first link in the chain.

In the foregoing statistics this view of the matter is not taken into consideration. The carrier is held responsible only for the first link.

For the attainment of complete statistics on the sources of typhoid infection it is necessary that the epidemiologist should not be content to stop his enquiries at the point where he has been able to demonstrate a case of typhoid fever as the immediate source of infection.

These considerations have been insisted upon by Schumacher (1909) in a recent report on endemic typhoid fever at Cröv, in the district of Trier. He comments on the fact that according to Frosch's collected figures only 47·4 per cent of the total cases were explained, and contends that the percentage of cases due to carriers would probably have been found to be much higher had the investigations of the epidemiologist and the bacteriologist been prosecuted with greater insistence. The bacteriological work carried out in connexion with endemic typhoid fever at Cröv, a small typhoid-ridden village, containing about 1,750 inhabitants, was limited only by the reluctance exhibited by a few families to provide material for examination, and even this appears to have been successfully overcome. It is impossible here to detail the whole course of the investigations. The original paper must be consulted and will repay careful study as it is fully provided with charts of the village showing the houses in which cases of typhoid fever occurred in the different years, and those houses in which carriers were resident. I must confine myself here to the actual statistics.

During the period 1903–1908, 45 cases in all occurred. Of this total only 24, *i.e.*, 51·1 per cent had been explained by previous enquiries. As the result of the extensive bacteriological work carried out by Schumacher in the village, practically all the 45 cases received adequate explanation. The following are the figures relating to the different modes of infection:—

Imported cases... ...	6 = 13·4	per cent.	(Previous enquiry 4).
Contact with typhoid cases	20 = 44·4	„	(„ „ 20).
Cases in which it was doubtful whether the infection arose from carriers or typhoid cases	7 = 15·6	„	(„ „ 0).
Contact with carriers ...	12 = 26·6	„	(„ „ 0).

Schumacher says that "the discovery of the chronic carrier gave the key to the explanation of endemic typhoid in Cröv." The large percentage of 26·6 per cent is in striking contrast to that of Frosch (quoted above), and Schumacher suggests that the explanation of the discrepancy is to be found in the following considerations:—

(*a.*) The proportion of explained cases depends on the time that can be spent on the enquiry, on the persistence with which the bacteriological work can be carried out, and finally on the willingness of the people concerned to supply samples for examination. In Cröv these conditions were fully satisfied, whereas the collected data of Frosch were certainly not based on work of such uniform completeness.

(*b.*) It frequently happens that the responsible carrier cannot be detected till some considerable period has elapsed, and when, possibly, the statistics have been already made up.

(*c.*) The statistics only take account of the fact that the first link in a chain of cases was attributable to a particular carrier, whereas the whole chain of cases should really be put to the charge of the carrier if the importance of the latter is to be rated at its true value.

If in the figures for Cröv this latter consideration was taken into account, the number of cases directly due to carriers (viz., 12) would have received an accession of eight indirect cases, giving a total of 20, *i.e.*, 44·4 per cent. These additional eight cases were due to infection from typhoid cases in chains started by carriers.

I close this chapter with the data collected by G. Mayer (1910), regarding endemic typhoid fever in the Bavarian Pfalz. The bacteriological work was carried out apparently in the most complete manner, and to Mayer we are indebted for many important and elemental facts with regard to intermittency and the occurrence of typhoid bacilli in the excreta during the incubation period. In previous chapters many of these data have been referred to. Here I give Mayer's figures relative to the infections caused by carriers :—

—	Number of Infective carriers.	Cases of Typhoid directly due to these.	Site of Infection.					
			In dwellings.	Business.	Bureau.	Social Intercourse.	School.	Shops dealing in food stuffs.
1904 ...	19	63	17	1	2	3	5	4
1905 ...	12	33	12	—	2	—	2	2
1906 ...	25	43	19	—	—	2	3	3
1907 ...	16	21	14	—	—	—	1	1
Total	72	160	62	1	4	5	11	10

During this period there was a total of 495 endemic cases, for 160 or 32·3 per cent. of which carriers were held responsible. As will be seen this figure corresponds fairly closely with that obtained by Schumacher.

With regard to the conditions under which the carriers were infective, the table shows that the great majority of the infections due to carriers arose in the domestic circle, while the school and food shops (bakery, dairy, inns, &c.) constituted a good second. In Mayer's view the unclean hand of the carrier is in most cases the agent which transfers infection to the new host.

CHAPTER XIV.

IMMUNITY QUESTIONS IN CARRIERS.

In previous chapters incidental references have been made to the antibodies demonstrable in the serum of the typhoid-carrier. For diagnostic purposes, at least, the agglutination test has hitherto proved of most service, and I have already discussed the value of this reation and its limitations in Chapter XI.

Here I propose to enter a little more fully into the immunity side of the carrier question in so far as the recorded facts warrant.

In the first place with regard to the agglutinins, about two-thirds to three-quarters of all chronic carriers give a well-marked Widal reaction (titre of 1 in 100 or at least 1 in 50). Some, indeed, have been found to exhibit a very high agglutinin content (up to 1 in 2,000 or higher), but such high titres are generally associated with an intercurrent acute infection or auto-infection such as cholecystitis.

Owing in great measure to the reluctance of healthy carriers to furnish specimens of serum and the insufficient facilities for work of this nature in institutions where carriers are isolated, our knowledge of the variations in the agglutinin-content of carrier-sera over a long period, is very deficient. An investigation of this matter might yield results of great value.

With regard to the transitory carrier who has never had any obvious symptoms of typhoid fever or who has so far not developed symptoms, definite statement as to the course of the agglutinins cannot yet be made. We know that typhoid bacilli may be excreted in the fæces and may even be circulating in the blood-stream for some considerable time before the agglutinins make their appearance in the serum. This fact may explain the recorded absence of a Widal reaction in a certain proportion of transitory carriers. On the other hand, a development of agglutinins has been observed to occur in the so-called "symptomless" cases of typhoid fever (Lentz, Scheller, already cited), who are found to discharge bacilli for very short periods. It is important to remember these points in those cases in which the physician has a positive reaction reported to him, which however, does not appear to be associated with any definite symptoms of the disease. Such cases undoubtedly occur and may give rise to considerable scepticism as to the value of the Widal test. For the satisfaction of the physician and the bacteriologist, an attempt should always be made to examine the excreta in view of the possibility of such cases being really temporary carriers.

I have already discussed certain other limitations of the Widal test in carriers, particularly its not uncommon occurrence in cases of miliary tuberculosis which do not exhibit typhoidal lesions at autopsy. In this type of case the excreta should always be bacteriologically examined, especially in children, in whom notoriously the course of typhoid may be atypical. It would take too much space to enter into the question of positive Widal results either in typhoid-carriers who also harbour organisms of the Gaertner-paratyphoid group or in persons infected with members of this group only. The presence of a co-agglutinin for B. typhosus in the serum of food-poisoning cases is now well established, though no satisfactory explanation has hitherto been given. In this monograph I have purposely avoided the discussion of mixed infections (typhoid with paratyphoid, &c.), in view of the present unsettled state of opinion with regard to the etiological importance of this latter group.

One other point relating to the agglutinins in carrier-sera has to be observed. The serum of the carrier may agglutinate with ease the bacilli of a laboratory strain, but may have little or no influence on the homologous strain. It must be noted, however, that the reaction with the homologous strain may occur late, the velocity of reaction being much slower than with the stock strain.

Ledingham (1908) recorded the results with two carrier-sera tested, both with the stock strain and with the homologous and other carrier strains. One of them gave a marked reaction with the laboratory strain only, but with the homologous strain and another carrier strain there was merely a trace of agglutination after nine hours. On the other hand another carrier serum was able to agglutinate with equal ease all three strains. Kennedy (1910) records similar results.

In those carriers in which no agglutination of the homologous strain takes place, one cannot assume that the serum contains no suitable receptors of any kind for this strain, as we know that the serum may still possess a high opsonic or tropic content towards the homologous bacillus. Further, as we shall see, there may be no agglutinins in the serum either for stock or homologous strains and yet complement-deviating bodies may be demonstrable.

The influence of vaccination (with typhoid vaccines) on the agglutinin-content of carrier-sera varies greatly. In one case (Thomson & Ledingham (1910)) the titre rose from less than 1 in 20 to 1 in 800 towards the stock strain, and to 1 in 400 towards the homologous strain. Recently, however, I have had a case in which the agglutinins remained stationary even after a course of vaccination with the patient's own strain. Kennedy (1910) has recently published charts showing in two cases either no change or only a very insignificant rise in the agglutinins, and in one case a stationary titre followed by a marked rise to 1 in 300 after the use of a specific vaccine.

Bactericidal Substances.

Observations on the bactericidal power of the serum of carriers are few, and these go to show that little or no variation from the normal standard occurs.

On two occasions (Ledingham (1908)) I have tested the sera of three carriers against the homologous and other strains (in vitro tests). The sera were inactivated and complemented with fresh guinea-pig serum. Some increase in the bactericidal power of the serum was found over that of the control serum, but the differences appeared to depend largely on variations in the resistance of the strains employed.

A sufficient quantity of serum for experiments of this nature is not readily available. Niepratschk (*vide* Chapter VI.) tested by the Pfeiffer method the bactericidal power of the serum of his urinary carrier. The virulence of the carrier strain was raised by passage through the guinea-pig from one-quarter of a whole agar-culture to one-quarter of a loop (= minimal lethal dose for guinea-pig of 250 gms. by intraperitoneal inoculation). With this strain and the carrier serum he made the following experiment :—

Guinea-Pig.	Result.
A. ¼ loop + 1 c.c. of 1 in 200 dilution of serum.	Death after 24 hours.
B. ¼ ,, +1 ,, 1 ,, 100 ,, ,,	,, 24 ,,
C. ¼ ,, +1 ,, 1 ,, 50 ,, ,,	,, 24 ,,
D. ¼ ,, +1 ,, 1 ,, 25 ,, ,,	Lived.
E. ¼ ,, +1 ,, 1 ,, 10 ,, ,,	,,
F. ¼ ,, without serum	Death.

The bactericidal titre, therefore, lay between ·02 and ·04 and was thus very low.

Opsonic Substances.

Ledingham (1908) found a very marked increase in the opsonic content of carrier-sera towards homologous strains, indices of 4 to 9 being obtained. Further, this opsonic substance disappeared almost completely on inactivation of the serum, but was readily restored on complementing with fresh normal serum, which of itself had little opsonic value. An opsonic amboceptor was thus demonstrated in carrier-sera.

Gaehtgens (1909) examined 16 carrier-sera and found in all except one (an intermittent case) a marked increase in the opsonic content. He also tested the sera of a number of persons who had had enteric at varying periods previously, but who were not carriers. An increase of opsonic power could be demonstrated only in those whose attack dated three or four months back.

In a recent communication Kennedy (1910) has reported a considerable increase in the opsonic content of carrier-sera. During vaccination a further steady rise takes place, which may not be accompanied by any definite increase in the agglutinin content.

Hamilton (1910) has also found abnormal opsonic indices in typhoid-carriers and recommends the opsonic tests in the preliminary search for carriers.

Complement-Deviating Substances.

Schöne (1908) investigated this question in three carriers and in the serum of two of these he was able to demonstrate quite definitely the presence of complement fixing-bodies. One of my colleagues—Henderson-Smith—(experiments not yet published) has also been successful in demonstrating these substances in the sera of two untreated typhoid-carriers, both of whom gave completely negative Widal reactions.

In concluding this chapter one feels compelled to admit that specific antibodies for the typhoid bacillus do pass over into the general blood stream in typhoid-carriers, although the vegetative foci may be considered to be in great measure shut off from or even, as some would suggest, entirely outside, the influence of the general circulation. The "local immunity" theory of Wassermann and Citron (1905) can only, therefore, afford a partial explanation of the prolonged vegetation of the typhoid bacillus in the gall-bladder and biliary tracts. Much work yet remains to be done on the immunity aspect of the carrier question.

CHAPTER XV.

Various Measures either Employed or Suggested to Diminish the Spread of Infection by Carriers.

In this concluding chapter I propose to discuss briefly the various precautions which have been adopted or recommended by sanitary authorities and others in order to reduce as far as possible the risk of infection from carriers. Pending the discovery of some efficient mode of therapy, all attempts to cope with this danger by sanitary measures are worthy of the most serious consideration at the present time. Obviously the first step is the adoption of some form of routine bacteriological examination during convalescence, and in previous chapters I have sufficiently alluded to the practice in vogue at the typhoid stations in Germany and elsewhere, and to the drawbacks from which practically every stereotyped routine must suffer, owing to intermittency, imperfection of bacteriological method, or both. Still there is no doubt that much good can be accomplished by the early recognition of carriers, and experience has shown that the longer the duration of bacteriological supervision the less is the risk of overlooking the intermittent carrier. Monthly examinations of the excreta of all convalescents for a period of one year would probably suffice, but in view of the great practical difficulties that such a scheme would involve, I do not propose to discuss it here.

Otto Mayer (1909) has suggested in a recent paper the foundation of Convalescent Homes for recovered typhoid cases. In such homes the convalescent who is still excreting the specific bacilli on discharge from hospital would be retained. By suitable treatment, dietetic and otherwise, by gymnastic exercises, &c., efforts would be made to encourage the physiological excretion of typhoid bacilli until possibly complete cessation resulted. Whereas many convalescents are compelled to resume their active duties at a far too early stage, when consequently the natural recuperative powers of the organism do not get an opportunity of throwing off an infection that is tending to become indolent, in the Convalescent Home every opportunity would be afforded to the bactericidal and antitoxic powers of the organism, of exercising their full effect. Full and accurate statistics would be kept regarding the duration and severity of the disease, the diet employed in convalescence and in the home, the muscular power of the patient and the bacteriological results. Such statistics would later prove of great value in deciding the influence exerted by the treatment during convalescence on the carrier-output.

There is no doubt that such institutions would prove of service in many ways. The patients that would ultimately have to be discharged in a potentially infective condition would be accurately instructed as to the precautions they should take on their return to civil life. This of itself would be a great gain, as the difficulty of impressing on unintelligent carriers the necessity of taking strict precautions as to disinfection has proved a serious stumbling block.

In institutions such as lunatic asylums the problem of dealing with chronic carriers who are also chronic lunatics is solved by the simple and successful expedient of isolation (*see* Chapter V.). This measure, however, may prove an expensive one, especially in the case of small institutions, as it may involve the upkeep of an isolation block with special attendants for a period coincident with the life of the patient.

Grimme (1908) has stated that prolonged isolation is unfavourable to the patient, as little or no intercourse is possible and the patients themselves do not see the necessity for the detention. This may certainly be true in some cases, but so far as the asylum cases that I have had under bacteriological supervision for two and a-half years are concerned, I am informed that isolation has had no prejudicial effect. It may be otherwise with acute lunatics who are carriers.

Every new patient, on entrance into the asylum, should be examined bacteriologically.

In the Army, measures have already been taken for dealing with known carriers. If, after a course of therapeutic treatment the carrier-condition persists, the soldier is discharged from service with or without a pension according as he agrees or not to the notification on his discharge-sheet, that he is a chronic typhoid-carrier. Drastic steps have also been taken to prevent the employment of regimental cooks who may happen to be carriers. The following "Standing Orders" for the Military Medical Services in India, 1908, I quote from a recent paper by Carmichael (1910), who enters a plea for the registration of typhoid-carriers in the army :—

> "No man who has recently suffered from enteric fever should be so employed (whose duties entail the handling of food intended for British troops, in kitchens, Officers' and N.C.O.'s messes, regimental and other institutions and clubs, government and regimental dairies, bakeries, mineral water factories, &c.) until it has been placed beyond all doubt, by repeated bacteriological examinations of fæces and urine that he no longer harbours the *Bac. typhosus*. In cases where means for carrying out such examinations are not available these men must not be employed."

Carmichael would propose the addition of this order to the Home Regulations with the wording "who has recently" altered to "who has ever."

At the Fleetwood station, Carmichael allows no man who is known to have suffered from enteric fever to be employed either in the kitchen or as orderly man. Certainly where facilities are not available for determining whether men who have had enteric fever, are carriers or not, this plan may be usefully adopted, but it does not exclude the risk of employing men whose primary infection may have been so slight as to remain unrecognised and who may quite possibly be chronic carriers.

Semple and Greig (1908), in the Indian Army advise the careful bacteriological examination of all men (Europeans and natives) before permitting them to be employed in connexion with the preparation and distribution of articles of food and drink.

In the civil population the problem of dealing effectively with carriers revealed in the course of enquiries into occurrences of enteric fever presents difficulties which only the future can solve. At present much good is being done in south-west Germany and elsewhere by retaining all carriers under bacteriological supervision, by giving suitable instruction with regard to disinfection of their excreta and their persons (particularly their hands), and by oral and verbal advice as to the occupations they should avoid. A useful series of "Standing Orders" employed in the Pfalz stations, accompanies a recent paper by Mayer, G. (1910). Of one of these, dealing with typhoid-carriers and convalescents, I give a translation. It has been in force since 1904.

1. Typhoid carriers and clinically cured cases are retained under bacteriological supervision until a bacteriological cure results.
2. So long as they discharge bacilli, the official disinfecters carry out or supervise the continual disinfection of privies used by them with milk of lime.
3. In the case of school children, workers in factories and such like, teachers, officials in state and private bureaus, these may carry on their respective duties provided that the schools, factories, &c., are provided with suitable wash-basins and soap. On commencing duty and on every occasion when the privy or urinal is visited, the hands must be cleansed.
4. In dwellings the disinfection of privies and urinals is systematically carried out by the official disinfecters (with milk of lime).
5. Typhoid carriers are to be restrained from the preparation and sale of food stuffs.

Instructive pamphlets are also issued to every newly-discovered carrier. The following is a free translation of that issued to carriers by the typhoid station at Strassburg (quoted from Gaehtgens (1910)).

VERHALTUNGS-MASSREGELN FÜR TYPHUSBAZILLENTRÄGER.

(*Instructions for Typhoid-carriers.*)

1. Typhoid fever in its severest form runs the course of a nervous fever. In its slighter forms it is accompanied by diarrhœal symptoms, but frequently the symptoms of the disease are scarcely noticeable.

It is caused by a specific bacillus—the typhoid bacillus.

2. The typhoid-patient harbours the typhoid-bacilli in his body, and discharges them during the disease with the stools and urine.

3. Some persons may continue to discharge typhoid-bacilli in the fæces for months or years after convalescence, or even although there has been no obvious primary attack. These persons are called typhoid-carriers.

4. Typhoid-carriers suffer as a rule from gall-bladder troubles, which give rise to transitory colic, jaundice and gall-stones, but frequently these symptoms are not present.

5. Carriers may infect other persons with typhoid fever just as typhoid-patients do.

6. Infection occurs most frequently by the hands, which are readily contaminated with typhoid bacilli during defæcation and urination. Infection may also be spread by soiled body- and bed-linen.

7. The bacilli get transferred from the unclean hands to other persons either by direct contact or by indirect contact, *e.g.*, with food-stuffs and various objects used by other persons.

8. It is possible for typhoid-carriers to reinfect themselves. In such cases one may expect an aggravation of the already existing gall-bladder troubles.

9. Carriers may avoid infecting other persons or themselves by the following precautions :—

(*a.*) The carrier must always exercise the greatest cleanliness.
(*b.*) Hands should be thoroughly washed on getting up in the morning, before every meal, and before touching food or drink (especially milk).
(*c.*) The carrier must, after using the water-closet, cleanse the hands thoroughly with soap and water or with a disinfectant. There should always be a sufficient quantity of closet-paper in the water-closet.
(*d.*) The carrier must have his own towel, which no one else may use.
(*e.*) The carrier's dirty body- and bed-linen should, before washing, be dipped in cresol-water (two tablespoonfuls of cresol-soap solution to one litre of water).
(*f.*) The carrier should, as far as possible, avoid taking part in the actual preparation of food or in its sale.

10. It is to the carrier's own interest that he or she should send, about once a month, a specimen of the stools and of the urine to the Bacteriological Institute at Strassburg in order that it may be determined whether the excreta still contain typhoid bacilli. The examination is done gratis. Suitable vessels for the reception of excreta are sent post-free from the Institute.

11. The Institute is very pleased to give advice regarding the disinfectant to be used by carriers.

12. The precautions advised above are absolutely indispensable, and it is morally incumbent on carriers to adhere to them in order to avoid infecting other people.

Davies and Walker-Hall (1908), of Bristol, have also issued a pamphlet containing instructions which, they suggest, should be given to typhoid convalescents. These are reproduced here :—

SUGGESTED INSTRUCTIONS TO TYPHOID CONVALESCENTS.

(*To be handed to Patients when Discharged from Hospital.*)

Typhoid fever is caused by a germ (the typhoid bacillus) which enter the body in food or drink or swallowed dust. When the convalescent stage is reached, the germ may remain in the intestines and cause relapses of the disease. Sometimes the germ remains permanently in the intestines, and may cause a return of the disease many years after the first attack. The germ may also induce the formation of gall-stones. Thus it is evident that the contents of the intestine of the typhoid convalescent are infective, and that the convalescent may be the unconscious means of transmitting the disease to his, or her, own family or friends. Cooks, male or female, dairymen or dairywomen, milk-vendors, greengrocers, butchers, fishmongers, provision dealers, workers in cocoa, chocolate, or confectionery, waiters and waitresses, and the mother who prepares food for the family, form a class of convalescents in which the opportunities of transmission of the disease are very frequent. The following provisional rules are suggested with a view to diminish the risk of infection :—

1. The hands and nails should be thoroughly washed, first in disinfectant solution, then in soap and water, and well rinsed before touching any foodstuffs, especially milk.
2. After the bowels are opened or the bladder is emptied, the hands and nails should be at once disinfected and washed.
3. Strong disinfecting solution should be poured over the stools, &c., before the plug of the water-closet is used or the lid of the dry closet is shut down.
4. When the motions are loose the risk of infection is increased and additional care should be taken.
5. The convalescent should periodically visit the medical attendant, so that the blood, &c., may be tested, and measures may be taken to control the action of the germs. As there is generally no need to deal with the drains, or to disinfect rooms or houses for these special cases, no upset of the domestic arrangements is necessary.
6. In the household where a patient is convalescing from typhoid fever, the additional precautions of boiling all the milk or water used for drinking or in the preparation of food should be undertaken, and uncooked foods should be avoided.

There is no doubt that much good has already been accomplished by instructing typhoid-carriers in proper methods of disinfection, and it is on the disinfection of the hands that chief stress must be laid. Gaehtgens (1910) has performed an interesting series of experiments designed to determine the most efficient and at the same time the least irksome method of cleansing the hands of typhoid-carriers. He smeared the hands and fingers with fæces containing typhoid bacilli, and determined the relative disinfectant values of mechanical washing, with and without disinfectants, and followed or not followed by thorough drying. He found that washing with soap and water alone, without subsequent drying of the hands, caused a marked fall in the number of B. coli and B. typhosus, especially of the former. If, however, the hands were dried thoroughly after removal of the soap in running water, subsequent cultivation frequently showed a complete disappearance of B. coli and B. typhosus.

For those carriers, therefore, who are not specially engaged in handling food-stuffs, the mechanical cleansing of the hands with soap and water and subsequent drying affords a tolerably complete protection. For those carriers on the other hand, whose occupation entails the handling of such material, it is advisable to employ an antiseptic after the ordinary washing and drying process in order to ensure complete removal of any typhoid germs still clinging to the hands. For this purpose Gaehtgens found that the most satisfactory disinfectant was alcohol either in the form of eau-de-cologne or spirits of wine.

APPENDIX.

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